South African Medical Journal
Suid-Afrikaanse Tydskrif vir Geneeskunde
P.O. Box 643, Cape Town — Posbus 643, Kaapstad

Cape Town, 17 August 1957
Weekly 2s. 6d.

Vol. 31 No. 33

Kaapstad, 17 Augustus 1957
Weekliks 2s. 6d.

GENERAL PRACTICE SERIES

DISEASES OF THE GONADS*

W. P. U. JACKSON, M.A., M.D., M.R.C.P.

and

R. HOFFENBERG, M.D., M.R.C.P.

From the Endocrine Clinic, Department of Medicine, Groote Schuur Hospital, and the University of Cape Town

Recent important advances in gonadal disorders include the application of methods of 'nuclear sexing', a clearer understanding of hermaphroditism, intersexuality and 'ovarian agenesis', and an appreciation of the frequency of hyperthecosis ovarii in secondary menstrual disorders. The treatment of undescended testes has been placed on a sounder footing.

1. EUNUCHOIDISM AND MALE HYPOGONADISM

The onset of puberty is heralded by increasing pituitary activity, as is indicated by rising gonadotrophin output. The testes respond to this by development of both seminiferous tubules and of Leydig cells. The latter produce testosterone, which in its turn induces secondary male characteristics and also acts 'thermostatically' on the pituitary, controlling gonadotrophin production by its inhibitory effect. Hence clinical hypogonadism may be the effect of a primary pituitary defect in which gonadotrophin production (measured by urinary F.S.H.) is low, or of a primary testicular defect in which gonadotrophin production is high, but the testes cannot respond to it.

The problem frequently presented to the practitioner is one of *delayed puberty*. Since perfectly normal puberty often occurs as late as the age of 16 (even up to 20 occasionally), there is no clinical reason for treatment under that age, unless there is collateral evidence of testicular damage. If there are no signs of puberty at all over the age of 16, the patient should be further investigated. His lack of development may be caused by a *primary testicular* or a *primary pituitary* disorder. In the former case, injection of gonadotrophins (e.g. 'Pregnyl') will be totally useless since the testes cannot respond. In the latter case, the continued use of testosterone, though producing male development, may condemn the patient to lifelong sterility, since no stimulation of seminiferous tubules will occur.

Over the normal age of puberty, the long limbs of eunuchoidism together with lack of male secondary characters indicate a hypogonadal state which started *before* pubertal age. If, however, the gonadal disorder started *after* puberty had occurred, the only complaints may be of infertility and shrinkage of the testes, sometimes with gynaecomastia. In all cases the differentiation of primary testicular and pituitary disorder is essential. (In the latter, gynaecomastia is very unusual.)

All this really means is that the practitioner should be able to diagnose hypogonadism, but cannot be expected to treat it without further specialized investigation of the basic cause.

Mumps not infrequently attacks the testes, and may damage them very severely. Any male, therefore, who develops mumps orchitis should be treated with cortisone or an analogue, while it is reasonable to add testosterone (one injection of 'depo-testosterone', 100 mg.) if the patient is adolescent or adult.

2. UNDESCENDED TESTES

Here it is vital to ascertain whether the testes are simply retractile or truly abnormally placed or fixed. The testes of all male infants should be examined at birth, since a retractile testis may be felt then, but not again for many years. The differentiation of these two conditions is often very difficult and an experienced paediatrician, paediatric endocrinologist or paediatric surgeon should be consulted. The true mal-descended testis requires operation, while the retractile testis will always descend later. Hormones are seldom indicated and certainly should not be used by the general practitioner.

* This is the last article in a series of 5 on endocrine disturbances by the same authors which have been appearing weekly.

3. GYNAECOMASTIA

This is quite common at puberty, and is often unilateral. It may not disappear on its own, and operation may be indicated if there is no regression after a year. Fat men develop 'pseudo-gynaecomastia' which is pure fat, and operation should not be recommended until general weight reduction has been achieved, when it may no longer be necessary. Other forms of gynaecomastia (except in the Bantu) are less common and need specialized investigation.

4. THE FAT BOY

Fat boys overeat, do not have delayed puberty, are not hypogonadal and suffer from no endocrine disorder. The disease is of the appetite, usually parentally induced. The apparently small penis becomes normal sized if the pubic fat is rolled back. The boys are often lazy and sleepy because of the soporific effect of too much food. This reduction in calorie expenditure itself induces further obesity. The patients need dieting (or, really, a more healthy diet), but it is usually more important to talk to the parents than to the children. You cannot expect to reduce a child's weight while the parents remain over 250 lb. apiece.

5. HYPERTHECOSIS OVARII

In this condition both ovaries are large and pearly white, with thick capsules, and contain multiple small cysts. This very common condition is found in combination with a variety of clinical phenomena.

1. The subject may be entirely normal gynaecologically.
2. There may be secondary amenorrhoea or oligomenorrhoea.
3. There may (less commonly) be menorrhagia.
4. The patient may be infertile.
5. There may also be hirsuties and obesity.
6. Sometimes real masculinization, with deepened voice, male hair distribution, powerful muscles and enlarged clitoris, develops.

There is much argument over the relation of the ovaries to the symptoms, but there is no doubt that the ovarian abnormality is common, particularly as a 'cause' of oligomenorrhoea with sterility. There is also no doubt that following wedge-resection of the ovaries many previously infertile women have conceived and their periods have become normal and regular. In these circumstances, and also in the true virilization group, it is important to be aware of the condition, and to resort to examination under anaesthesia or even to laparotomy if necessary for accurate diagnosis.

6. INTERSEX

No dissertation on the varieties of intersex will be attempted here. Intersex is, however, not uncommon (it has been reported to occur once in every 1,000 births) and the exact pathogenesis in every case must be worked out at an early age, if irremediable psychological harm is to be obviated. Consequently it behoves the practitioner or other person who delivers every baby to examine its genitalia carefully for any sign of intersexual development. Enlarged 'clitoris', hypospadias, non-descent of 'testes' in an apparent male may be as important as the obvious case in which there is a 'penis' with penile urethra together with a vagina.

Investigation of intersex may necessitate (1) the identification of the nuclear 'chromosomal' sex, (2) estimation of urinary 17 = ketosteroid output, (3) biopsy of any gonad, (4) visualization by opaque dye of the urinary and genital tracts, or (5) laparotomy.

It must be evident that, once again, the practitioner's role (and a very important one) lies in the recognition of an abnormality and in the referring of the patient for special investigation before he or she is 2 years old. The age of 2 is mentioned because it has been shown that over this age the child begins to develop an awareness of the sex in which it is being reared, and any subsequent change may result in very severe psychological distress.

7. OVARIAN AGENESIS (GONADAL DYSGENESIS)

We are beginning to think that 'ovarian agenesis' is the commonest cause of primary amenorrhoea. It is often, but not always, associated with shortness of stature and developmental anomalies such as webbing of the neck, a low nuchal hairline, or an asymmetrical face. Anyway it should be suspected in all cases of primary amenorrhoea, whatever the height or appearance of the patient.

The certain diagnosis, again, is a matter for the specialist. Most cases actually show *male* nuclear sex chromatin (i.e. the 'ovarian' agenesis in them is 'testicular' agenesis). Laparotomy may be necessary to establish the diagnosis.

This condition is important to recognize, because 'menstrual' bleeding, together with breast development and other advantages can be obtained from the long-continued cyclical use of oestrogens. Furthermore it is necessary to inform the patient that she can never become pregnant.

FEDERAL COUNCIL ELECTIONS

The further results[1] of the recent 5-yearly Branch elections for Federal Council which have been received at the time of going to press, show that the following candidates have been elected:

Cape Eastern
L. R. L. Solomon.

Cape Midlands
A. P. Albert.
L. E. Lane.
M. A. Robertson.

Vaal River
W. Chapman.

Orange Free State and Basutoland
F. Hagen.
D. J. Serfontein.
R. Theron.
G. F. C. Troskie.

Transkei
E. R. Louw.

1. Federal Council Elections (1957): S. Afr. Med. J., **31**, 785 (3 August).

South African Medical Journal

Suid-Afrikaanse Tydskrif vir Geneeskunde

EDITORIAL

PIGMENTATION AND MSH

MSH (melanocyte-stimulating hormone), also known as intermedin, melanophore-expanding hormone, and melanin-dispersing hormone, is found in the pars intermedia of the pituitary gland. It has been recognized for some 35 years to be the hormone responsible for controlling the darkening of the skin of the frog and other amphibia. Such darkening of the skin occurs in a dark environment, while in a bright environment the skin again becomes lighter. This increased pigmentation has been clearly shown to be caused locally by a dispersion of melanin within the melanocyte. The hormone is undoubtedly present in the pituitary glands of mammals also, but no such clear effect has hitherto been ascribable to it. It does appear, however, that melanin can be formed in the melanocyte of the skin of mammals (including man) and that extracts of pituitary glands containing much MSH activity can stimulate an increase in the amount of melanin in the skin.

The old teaching was that the pigmentation of Addison's disease was caused by a deviation of tyrosine from adrenalin formation (the adrenal being no longer able to elaborate adrenalin) to melanin formation, for which the adrenal gland was not necessary. This theory, however, was without any foundation in fact, so that it was natural that investigators should wonder whether MSH might not have something to do with the pigmentation. In fact, a high level of MSH activity has been found in the blood of patients suffering from Addison's disease. Similarly, MSH activity has been found to be excessive in Cushing's syndrome, in pregnant women, and in certain states of stress. In all these conditions, incidentally, an excess of circulating corticotrophin (ACTH) is also to be expected (although the relation of Cushing's syndrome to ACTH is still uncertain at the present time). In Addison's disease the low blood concentration of corticosteroids releases the inhibition to formation of ACTH in the pituitary. The demonstration of a close connection between MSH and ACTH was taken further by the fact that the most highly purified samples of ACTH still retained MSH activity. It was even suggested that ACTH and MSH might actually be the same thing.

That ACTH and MSH were distinct substances was soon shown by the almost complete separation of their activities;

VAN DIE REDAKSIE

PIGMENTASIE EN MSH

MSH (melanosiet-stimulerende hormoon), ook bekend as intermedien, melanofoor-uitdyende hormoon en melanien-verspreiende hormoon, word in die pars intermedia van die skildklier gevind. Vir ongeveer 35 jaar bestaan die wete dat dit die hormoon is wat vir die beheer van die verdonkering van die vel van die padda en ander amfibieë verantwoordelik is. Sodanige verdonkering van die vel geskied in 'n donker omgewing, terwyl die vel in 'n helder omgewing weer ligter word. Dit is duidelik getoon dat hierdie toename van pigmentasie plaaslik veroorsaak word deur 'n verspreiding van melanien binne-in die melanosiet. Die hormoon is ongetwyfeld ook in die skildkliere van soogdiere aanwesig, maar geen soortgelyk duidelike uitwerking is tot nog toe daaraan toegeskryf nie. Dit skyn egter dat melanien wel in die melanosiet van die vel van soogdiere (insluitende die mens) gevorm kan word en dat uittreksels van skildkliere, wat baie MSH-werking bevat, 'n vermeerdering in die hoeveelheid van melanien in die vel kan stimuleer.

Die ou leer was dat die pigmentasie by Addision se siekte teweeggebring is deur 'n afwyking van tirosien wat veroorsaak dat melanien, waarvoor die bynier nie nodig was nie, i.p.v. adrenalien, (aangesien die bynier nie langer in staat was om adrenalien voort te bring nie), gevorm is. Hierdie teorie was egter inderdaad ongegrond, sodat dit heel natuurlik was dat navorsers sou wonder of MSH-werking nie iets met die pigmentasie te doen het nie. 'n Hoë vlak van MSH-werking is inderdaad in die bloed van pasiënte, wat aan Addison se siekte ly, gevind. Soortgelyk is dit gevind dat MSH-aktiwiteit oormatig is by Cushing se sindroom, by swanger vroue, en by sekere toestande van spanning. Toevallig kan 'n oormaat van sirkulerende kortikotrofien (ACTH) ook by al hierdie toestande verwag word (alhoewel die verwantskap van Cushing se sindroom met ACTH tans nog onseker is). By Addison se siekte bevry die lae bloedkonsentrasie van kortikosteroïede die onderdrukking van ACTH-vorming in die skildklier. Die demonstrasie van 'n noue verwantskap tussen MSH en ACTH is verder opgehelder deur die feit dat die mees-gesuiwerde monsters van ACTH nog MSH-werking oorgehou het. Dit is selfs aan die hand gedoen dat ACTH en MSH inderdaad een en dieselfde is.

Dat ACTH en MSH afsonderlike stowwe is, is gou getoon deur die bykans algehele skeiding van hulle aktiwiteite; bowendien, sekere chemiese behandelings het die ACTH-aktiwiteit van die ‚hormoon' vernietig terwyl MSH-aktiwiteit

moreover, certain chemical treatments destroyed the ACTH activity of the 'hormone', while MSH activity was retained. Furthermore, different parts of the pituitary gland have very different ratios of activity of ACTH and MSH. Thus the anterior lobe is rich in corticotrophin while the posterior and intermediate lobes are rich in MSH. These differences of activity are of the order of 100 times.

Recently both ACTH and MSH (or at least, one variety of MSH) have been isolated and structurally analysed. Corticotrophin is apparently a peptide containing 30 amino acids in a long chain, while MSH contains some 18 amino acids, also in a single chain. A sequence of 7 amino acids is said to be identical in the two hormones, so that there is little wonder that their chemical properties are very similar and their separation very difficult. This similarity may even confer a basic melanocyte-stimulating property on pure ACTH, although very much weaker than that of pure MSH. Thus apparently pure corticotrophin subjected to complicated chemical alteration, and then partially regenerated, first lost and then recovered both ACTH and MSH activity—the two could not be separated. No amount of purification has been able to rid ACTH of a constant small amount of MSH activity, which really does, therefore, appear to be a property of the corticotrophin itself. Incidentally, commercial ACTH has a good deal more MSH activity than this basic amount, indicating its contamination with the MSH hormone. Now treatment of corticotrophin with periodate has been found to destroy its ACTH activity, while leaving intact the small moiety of MSH action. It is believed that this treatment attacked only the serine residue at the end of the corticotrophin peptide chain, leaving intact the 7 amino acids common to both ACTH and MSH.

We can now tentatively explain the pigmentation of Addison's disease and that following adrenalectomy as being caused by an increased production of MSH and ACTH, assuming that the output of both these hormones is regulated by the quantity of circulating corticosteroids of the cortisone type. On treatment with cortisone or hydrocortisone some depression of production of these hormones occurs and the pigmentation lightens, although it does not entirely disappear. In Cushing's syndrome, and in pregnancy, pigmentation may again be correlated with high ACTH and MSH production, this time with increased adrenal function also. In panhypopituitarism the skin colour may become paler and the patients no longer tan in sunlight. The pituitary ACTH and MSH production is here suppressed by local disease, and no change is brought about by treatment with replacement hormones. The clinical issues, however, are by no means clear cut, and we must await further elucidation along these lines.

A large number of workers have contributed to work in this field, and the interested reader is referred to the Brit. Med. J. 20 *April* 1957, *p.* 935, *for a list of references. For easily accessible reviews:*

Syndor, K. L. *et al.* (1953): J. Clin. Endocr., **13**, 891.
Shizume, K. and Lerner, A. B. (1954): *Ibid.*, **14**, 1491.
Lee, T. H. and Lerner, A. B. (1956): J. Biol. Chem., **221**, 943.

behoue gebly het. Boonop het verskillende dele van die skildklier hoogs verskillende aktiwiteitsverhoudings van ACTH en MSH. Aldus is die voorste lob ryk aan kortikotrofien terwyl die agterste en tussenlobbe ryk aan MSH is. Hierdie verskille van aktiwiteit is in die verhouding van 100-maal.

Onlangs is beide ACTH en MSH (of, ten minste, een soort van MSH) afgesonder en volgens struktuur ontleed. Kortikotrofien is blykbaar 'n peptied wat 30 aminosure in 'n lang ketting bevat, terwyl MSH ongeveer 18 aminosure, ook in 'n enkel ketting, bevat. Dit word beweer dat 7 aminosure, wat mekaar opvolg, identies by beide hormone is, sodat dit glad nie verbasend is dat hulle chemiese hoedanighede baie eenders en hulle skeiding baie moeilik is nie. Hierdie eendersheid mag selfs 'n basiese melanosiet-stimulerende hoedanigheid aan suiwer ACTH verleen, alhoewel dit baie swakker as dié van suiwer MSH sal wees. Op hierdie wyse het suiwer kortikotrofien, onderworpe aan ingewikkelde chemiese verandering en dan gedeeltelik geregenereer, blykbaar eers beide ACTH- en MSH-werking verloor en dit dan teruggewen—die twee kon nie geskei word nie. Geen mate van suiwering was daartoe in staat om ACTH van 'n konstante klein hoeveelheid van MSH-aktiwiteit te bevry nie. Dit skyn dus of dit werklik 'n hoedanigheid van die kortikotrofien self is. Terloops, handels-ACTH het heelwat meer MSH-aktiwiteit as hierdie basiese hoeveelheid, wat die vermenging daarvan met die MSH-hormoon aandui. Dit is nou gevind dat behandeling van kortikotrofien met perjodaat die ACTH-aktiwiteit daarvan vernietig, terwyl die klein mate van MSH-werking ongeskonde bly. Die mening is dat hierdie behandeling slegs die serien-oorskot aan die end van die kortikotrofien-peptiedketting aanval en die 7 aminosure, wat beide ACTH en MSH in gemeen het, onaangetas laat.

Ons kan nou voorlopig die pigmentasie van Addison se siekte en dié wat op adrenalektomie volg, verklaar deur te sê dat dit deur 'n vermeerderde vervaardiging van MSH en ACTH veroorsaak word, indien ons aanneem dat die produksievermoë van beide hierdie hormone deur die hoeveelheid sirkulerende kortikosteroïede, van die kortisoon tipe, gereguleer word. By behandeling met kortisoon of hidrokortisoon vind 'n sekere mate van onderdrukking van die vervaardiging deur hierdie hormone plaas en die pigmentasie word ligter, alhoewel dit nie heeltemal verdwyn nie. By Cushing se sindroom en by swangerskap kan pigmentasie weereens met 'n hoë ACTH- en MSH-vervaardiging gekorreleer word, nou ook met vermeerderde bynierwerking. By panhipopituitarisme mag die kleur van die vel ligter word en die pasiënte brand nie meer bruin in sonlig nie. By hierdie toestand word die ACTH- en MSH-vervaardiging deur die skildklier deur plaaslike siekte onderdruk en die toestand verbeter geensins deur behandeling met verplasingshormone nie. Die kliniese beslissings is egter glad nie baie duidelik nie, en ons moet wag op verdere opheldering in hierdie rigting.

'n Groot aantal navorsers het bydraes gelewer tot werke op hierdie gebied, en die geïnteresseerde leser word verwys na die Brit. Med. J. *van* 20 *April* 1957 *vir 'n lys van verwysings. Vir maklik-bekombare oorsigte:*

Syndor, K. L. *et al.* (1953): J. Clin. Endocr., **13**, 891.
Shizume, K. en Lerner, A. B. (1954): *Ibid.*, **14**, 1491.
Lee, T. H. en Lerner, A. B. (1956): J. Biol. Chem., **221**, 943.

GLUCAGON

The name glucagon was applied as early as 1923[1] to a hyperglycaemic factor (HGF) present in certain extracts of the pancreas. Since that time, and particularly in more recent years, much work has been done in order to establish the site of origin of this substance, its role in the regulation of carbohydrate metabolism and in relation to the action of insulin, and indeed whether it is really a hormone at all. There have been conflicting reports in the literature which render the status of glucagon in some respects unsatisfactory.[2]

Glucagon has been extracted not only from the pancreas but also from other tissues such as the gastric and duodenal mucosa, and some claim to have demonstrated its presence in the urine. It can be extracted after destruction of the beta cells of the islets by alloxan. For a number of years it has been stated that glucagon comes from the alpha cells of the pancreas, and while some workers state that it is not exclusively manufactured by these cells the evidence on the whole is overwhelming in favour of this site as the place of origin for this hyperglycaemic factor.

The question whether glucagon is an antagonist or synergist of insulin has led to controversy. A number of the activities of glucagon are opposed to the metabolic actions of insulin, for example in the liver. In the peripheral tissues the situation is more complicated; some regard glucagon and insulin as synergistic in action, others have demonstrated that glucagon has anti-insulin actions at this level. One explanation put forward to account for the apparently paradoxical findings is the fact that preparations containing glucagon may contain insulin. It is clear that even more highly purified crystalline glucagon will need to be used in all studies with this compound. If glucagon is a hormone its peripheral effects are probably secondary. After leaving the pancreas it enters the liver, where it is rapidly inactivated; little will escape to act on the peripheral tissues.

The hormonal status of glucagon is still uncertain, but it presents a strong appearance of being a hormone. There is not only indirect but also direct evidence that it is secreted into the blood stream; for example, a hyperglycaemic factor has been demonstrated in the pancreatico-duodenal blood. It is a polypeptide of fairly low molecular weight like certain hormones. It is produced in the islets of Langerhans. It has powerful and specific effects on various metabolic processes, for example in the liver, in extremely low concentrations. The liver has a powerful inactivating mechanism for the substance. All these points strongly suggest that glucagon is a hormone.

While many may regard our present knowledge concerning glucagon as inconclusive, the weight of evidence appears to place it as a hormone, formed most probably in the alpha cells of the islets of the pancreas, and acting as a powerful hepatic antagonist or corrector of insulin.

1. Gibbs, C. B. F. *et al.* (1923): Quart. J. Exp. Physiol. suppl. **13**, 128.
2. Editorial (1956): Brit. Med. J., **2**, 288.

ENDEMIC SYPHILIS OR YAWS?

A REVIEW OF THE LITERATURE FROM SOUTH AFRICA

J. F. MURRAY, M.D.

Pathologist, South African Institute for Medical Research, Johannesburg

The first reference to the treponematoses in Southern Africa appears to be a statement by Lichtenstein[1] that, during his travels in Southern Africa between 1802 and 1806, he could find no evidence of syphilis amongst the Xhosas. Livingstone[2] in his reference to the Bechuana in 1857 stated that the disease was 'unable to maintain itself in any permanent form in persons of pure African blood anywhere in the centre of the country', but by 1885 Warren's expedition into Bechuanaland[3] found the Natives badly infected. From 1881[4] and onwards the disease appears to have spread rapidly and by 1887[5] the district surgeon of Bedford stated that more than half of 5,529 Natives examined by him were syphilitic.

An interesting and possibly a unique aspect of syphilis in South Africa is the statement by Mitchell[6] that 'a Chief in the Northern Transvaal was so impressed by the ravages of syphilis amongst his people and with the efficacy of inoculation or vaccination against smallpox, that he caused some 300 or 400 members of his tribe to be inoculated with material from an infective case of syphilis'. The results are not recorded.

The first clinical description of a case of treponematosis which we have been able to find in the early South African medical journals is by G. A. Heberden[7] of Barkly West, who described a case which he diagnosed as 'Frambesia or yaws.' The lesions, which were papulo-pustular, condylomatous, and polymorphous in nature occurred mainly on the head, neck, and face but were also scattered about the body and in the axillae and folds of the skin. The patient, a Bechuana, stated that he had seen many similar cases in Bechuanaland. Although Heberden classified the case as one of yaws it seems probable, in the light of modern knowledge concerning the treponematoses, that it was one of endemic syphilis. For 20 years there raged in the South African medical literature a lengthy, wordy and sometimes acrimonious controversy as to the exact nature of the treponematosis which was widely spread in Southern Africa and particularly in Bechuanaland. So heated did the discussion become that when McArthur and Thornton[8] asked the question, 'Is it necessary for there to be a primary chancre? Might it not be possible for the disease to be spread without a chancre at all?' Mathias[9] replied 'that the days of well authenticated miracles are well past and will probably never

come again, even in the interests of the District Surgeons of South Africa.'

On the one hand Mathias,[9-12] Hugo,[13, 14] Ricono[15] and Knobel[16] stoutly maintained that the condition was yaws, whereas McArthur and Thornton,[8] Cairns[17] and Walker[18] with equal confidence stated that the disease was syphilis. Mathias,[10] one of the most prolific writers on the subject, was emphatic that the condition was yaws. When confronted with Jonathan Hutchinson's dictum that yaws is 'syphilis modified by race and climate' Mathias thundered that 'it was only Hutchinson's great reputation as an authority on syphilis that maintained the existence of such an error for so many years, and made the attempts of others to preach the truth on this subject practically futile, and I believe that it is this alone which today accounts for the fact that yaws is practically not recognized.' The controversy is interesting in view of the fact that even today, 40 years later, despite our increased knowledge, dispute still exists about the exact relationship between these two treponematoses.

The opinion of McArthur concerning its exact pathogenesis varied from time to time although he was one of the most accurate observers of the condition. In his publication of 1911[8] he emphasized that the disease was transmitted from patient to patient by direct or indirect non-sexual contact and that it occurred mainly in childhood. Indeed, he gave an accurate and detailed report which differed in no important respect from the description of endemic syphilis by Hudson[19] in Iraq 25 years later. Although McArthur regarded late heredo-syphilis as an important feature in relation to the disease in Natives he thought that contact transmission was even more important. By 1922,[20] however, he had apparently modified his opinion and regarded heredo-syphilis as so prevalent that direct modes of transmission seemed to be of little importance among the Bechuanaland Natives. This opinion he maintained throughout the remainder of his publications and his weighty opinion continued to have an effect upon the approach to the subject of all medical men in South Africa.

Summarizing the South African literature over the last 50 years the following picture emerges.

INTRODUCTION AND SPREAD OF SYPHILIS

The Bantu in Southern Africa before their contact with the European appear to have been free of syphilis (Sax,[21] Mitchell[22]). Contact with the European introduced the disease amongst them and its spread was accelerated by the opening of the Kimberley diamond mines.[4] Possibly as a result of their proximity to the mines and of the high proportion of the male population which undertook labour at the mines the disease became particularly prevalent amongst the Bechuana. McArthur and Thornton[8] state that in 1904, of a population of 68,000 in Bechuanaland (excluding Gordonia), 12,000-14,000 were in employment on the Kimberley diamond mines annually.

According to Kark[23] living conditions of Africans in the Kimberley area were conducive to the spread of syphilis. Drunkenness was common, compounds were often filthy, and there was a rapid movement of men to and from the diggings. He emphasizes that a large number of men were living under abnormal social conditions and that promiscuity and prostitution were rife. As a result, by the turn of the century, the population was apparently heavily infected with syphilis, so much so that a Commission to report upon contagious disease amongst the Natives was appointed by the Government in 1906. The Commission[4] found that syphilis appeared to have been introduced somewhere in 1881, probably from Kimberley, and thereafter became widely prevalent so that its incidence varied from 'very little' to 'over 80% in some parts of the Zoutpansberg'. The Commission commented upon the varying incidence of the disease in different parts of the country but stated it to be 'enormously prevalent in the adjacent part of Bechuanaland'. They noted that the number of cases of syphilis and venereal disease treated at the Rietfontein Lazaretto in Johannesburg increased from 58 in 1900 to 659 in 1906.

At an intercolonial conference held in 1906 it was stated that syphilis was prevalent throughout the Native and Coloured races, that in some areas it was extremely prevalent and was increasing, that it was frequently imported by labourers returning from labour centres, that it was occasionally spread by servants to White persons, especially children, and that when it came under observation it was usually in the late tertiary state.

Almost all authors were convinced of the wide prevalence of syphilis amongst the Natives, but Leipoldt[24] expressed some doubt upon this point in 1920, mainly on the grounds that any estimate of incidence amongst the Bantu was seriously handicapped by the absence of accurate medical statistical information.

SEROLOGICAL FINDINGS

The first report upon the serological status of a Bantu population was that of Pijper,[25] who carried out Wassermann tests on 500 Coloured people at the Pretoria Hospital. The patients were of all ages between 6 and 60 and the sexes were about equally represented. The great majority were pure Natives but there were 'also some half-castes and mixtures of all kinds'. *Prima facie* cases of syphilis were excluded, but no further selection was made. The majority of the blood specimens were taken from traumatic surgical cases and from non-syphilitic patients from the medical wards and out-patient department. Many relations and visitors also contributed to the number of specimens. The results showed strongly positive reactions in 36·8% of the specimens and a further 11·0% which were definitely positive. In a further series of 40 apparently completely healthy Natives from Bathal district he found 12·5% positive Wassermann tests.[25]

Subsequent serological surveys in Southern Africa have shown a relatively high seropositivity rate, although the actual rate has varied considerably in different parts of the country. Schultz,[26] in 1926 obtained 16·6% strongly positive results in 242 Native males. In 1927, at the South African Institute for Medical Research,[27] specimens from 1,200 healthy Native mine labourers showed seropositivity rates as follows: Xhosa 2%, East Coast 7%, Pondo 8·5%, Bechuana 22%, Basuto 29·5%.

In 1937-39 Native males examined at the pass office in Benoni[28] showed 0·5% suffering from infective venereal disease. There were 5·0% showing superficial signs of old infections and 28·0% had a positive Wassermann reaction. The seropositivity rate among non-European ante-natal clinic patients in the same town was 35-42%.

Kark,[23] in 1949, concluded that few countries could have a higher incidence of syphilis than South Africa. Kark and

Le Riche,[29] in 1938-39, found 23·6% positive Wassermanns amongst African school children. Purcell,[30] in 1940 indicated that 'the incidence of syphilis in the Union is enormous'. Kark,[23] in 1949, reviewed the South African literature on seropositivity in various African groups and showed that it varied from 2·0% to 47·8%. The Annual Medical Report[31] of the Bechuanaland Protectorate Government for 1946 reported a seropositivity rate of 64% in 377 out-patients at Mahalapye.

After the introduction of serological tests the controversy whether the condition was yaws or syphilis appears to have died away in the South African literature and the high seropositivity rate amongst the Bantu was accepted as evidence of syphilis.

But it is not uncommon to find in private conversation that doubt is expressed about the interpretation of positive serological tests as evidence of syphilis. It has been felt by many that, owing to the numerous well-known biochemical aberrations found in any series of Bantu sera, many of the reactions might be biological false positives.[29] No method of testing this suggestion has been available until recently, but an investigation into this aspect of the problem has been proceeding at the Institute for Medical Research during the last 2 years and will be reported in detail in due course. Suffice it to state that the use of the *Treponema pallidum* immobilization (TPI) test and of a battery of serological tests for syphilis (STS) has confirmed the high seropositivity rate found by previous workers amongst the Bantu and has shown that, if one accepts a positive TPI as indicative of past or present treponemal infection, then a high rate of such infection exists amongst the Bantu.

CLINICAL MANIFESTATIONS

Reference is made above to the fact that the first case of treponematosis recorded in the early South African medical journals was described as yaws and subsequent publications were divided on the issue whether the common treponematosis seen in Southern Africa was syphilis or yaws.

The clinical picture (Ricono,[32] Garrow,[33] Hugo,[13, 14] Mathias,[9-12] Walker,[18] Heberden,[7] McArthur and Thornton,[8] Knobel,[16] McArthur[20]) was characterized by the presence of a papulo-pustular eruption (sometimes acuminated), condylomata in the flexures and moist areas of the skin, mucous patches in the mouth and throat, and periostitis, particularly of the legs and arms.

A notable fact was that these signs were seldom preceded by a primary chancre. Garrow[33] mentions that the condition sometimes originated sexually and then spread innocently, as in a group of farm workers which he described. McArthur and Thornton[8] refer to 27 cases spread commensally amongst children in a children's home in Kimberley. They regarded many cases of the condition as hereditary but they admitted that the usual stigmata of hereditary syphilis were absent. While they regarded sexual spread as important in the urbanized African, they felt that in the rural Bantu indirect spread by the use of common utensils and clothing was much more important. In the tertiary-stage destructive gummatous lesions occurred in the skin, nasopharynx and bones, but the viscera were seldom affected, cardio-vascular complications seldom occurred, and there were, apparently, no remote central-nervous-system complications such as tabes dorsalis and general paralysis of the insane. The destructive lesions of the nasopharynx sometimes became very extensive[14] and resembled the cases of mutilating endemic syphilis which have been described by Jones.[34] The lesions, which were clearly the tertiary lesions of endemic syphilis, were sometimes described as late manifestations of congenital syphilis (Hill-Aitken[35]).

Another feature of the condition was that not infrequently the lesions spontaneously healed and all authors affirm the rapid response to such antisyphilitic measures as potassium iodide, iodiform ointment, mercury and (at a later date) arsenical injections.

The association of a favoid condition of the scalp was, by some authors, regarded as a syphiloderm (McArthur and Thornton,[8, 20] Marshall and Wilson,[36]) but others regarded it as a favus infection (Mitchell and Robertson[37], Murray *et al.*[38]).

Those who felt that this treponematosis was yaws based their opinion upon the following facts:

(*a*) That a primary chancre was seldom observed,

(*b*) that there was little or no evidence of sexual spread,

(*c*) that it occurred most frequently in childhood,

(*d*) that there were no multiform eruptions,

(*e*) that the internal organs were seldom affected,

(*f*) that there was no iritis,

(*g*) that no central-nervous-system sequalae such as general paralysis of the insane or tabes dorsalis occurred,

(*h*) that patients readily recovered under external applications such as iodiform ointment, and some without any treatment at all, and

(*i*) that no hereditary manifestations were found in the offspring.

It is now known that all these arguments are equally applicable to endemic syphilis (Hudson,[19] Grin,[39] Guthe and Willcox[40]) and it is clear that the condition which was so widely spread amongst the Bantu of Southern Africa was endemic syphilis and not yaws. In recent years clinical descriptions of endemic syphilis have been published from Southern Africa (Murray *et al.*,[41] Willcox,[42] Taylor[43]). The disease still, apparently, occurs in the more remote parts of the subcontinent and is identical with the treponematosis described in earlier writings as yaws.[9-16] This is not to say that yaws has never occurred in Southern Africa, but the only authentic examples of it which appear in the South African literature (Hackett,[44] Bensusan[45]) clearly indicate that the disease had been imported from one or other of the endemic yaws areas in tropical Africa.

ETIOLOGY AND PREVENTION

The introduction of better hygiene of schools and of water supplies is, apparently, in itself sufficient to diminish the incidence of endemic syphilis in a primitive community. This has been exemplified in Southern Africa, where the incidence of the condition was found by Murray *et al.*[41] to be appreciably higher in the more backward areas of Bechuanaland as compared with the more advanced sections of the community.

It is of interest to note that, although penicillin was as yet unknown, McArthur and Thornton[8] as early as 1911 realized the value of mass therapy in the control of endemic

syphilis. They recognized the response of cases to minimal therapy and suggested that 'the difficulty of dealing with syphilis will disappear, for all that will be necessary is for each patient, and for any who react to the serum tests, to be injected with the solution of the new drug (606). And if the serum diagnosis cannot be simplified so as to become a practical measure, but Ehrlich's remedy stands the test of time, we consider that, in order to eradicate the disease, the Government might perhaps be justified in seeking from the Legislature powers to order the injecting of the new drug into every member of the known syphilitic families in this area'.

In rural areas of the Union standards of living amongst the Bantu have apparently advanced sufficiently to diminish appreciably the incidence of endemic syphilis amongst them. Even in the Native urban townships, insanitary and unhygienic though many of them are, the incidence of endemic syphilis is relatively low and only minor outbreaks occasionally occur. (Taylor,[43] Sachs,[46] Murray *et al.*[41]). The place of endemic syphilis in the South African community is apparently being taken by the classical venereal form of the disease, but the incidence of the latter, together with the occurrence of occasional sporadic outbreaks of endemic syphilis, is sufficiently high to maintain a high seropositivity rate amongst the Bantu of Southern Africa.

No satisfactory comparative studies have been carried out in the Union to determine the relative incidence of seropositivity in different sections of the Bantu population, such as school children compared with non-school children, rural compared with urban Bantu, various age groups, and so forth. A careful study of this type would give valuable information on the part syphilis is now playing in the Bantu populations of the Union of South Africa.

SUMMARY

The literature on syphilis in the Bantu of Southern Africa has been reviewed and the opinion is expressed that the condition frequently described in the past as yaws was, in fact, endemic syphilis. Cases of true yaws have been infrequent and have occurred only when imported from the tropical areas of Africa. The high rate of endemic syphilis in the past and the continuance of it in some foci, together with the occurrence of classical venereal syphilis, has led to a high seropositivity rate amongst the Bantu.

Use of the TPI test has confirmed that the high seropositivity rate found in the Bantu of Southern Africa is due to treponemal infection.

REFERENCES

1. Lichtenstein, H. (1812): Quoted by Sax, S. (1952): S. Afr. Med. J., **26,** 1037.
2. Livingstone, D. (1857): *Missionary Travels and Researches in Southern Africa*, p. 128. London: John Murray.
3. *Warren's Expedition.* Official Report. Quoted by McArthur, D. C. (1922): Amer. J. Syph., **7,** 569.
4. *Report of the Contagious Diseases Commission* (1907): Pretoria: Government Printer.
5. *Report of the Select Committee on Reports on District Surgeons* (1888): Quoted by Anning.[28]
6. Mitchell, J. A. (1926): Med. J. S. Afr., **21,** 210.
7. Heberden, G. A. (1898): S. Afr. Med. J., **5,** 274.
8. McArthur, D. C. and Thornton, E. N. (1911): S. Afr. Med. Rec., **9,** 18.
9. Mathias, J. (1911): *Ibid.*, **9,** 64.
10. *Idem* (1910): *Ibid.*, **8,** 102.
11. *Idem* (1911): *Ibid.*, **9,** 128.
12. *Idem* (1911): *Ibid.*, **9,** 174.
13. Hugo, D. de V. (1911): *Ibid.*, **9,** 41.
14. *Idem* (1915): *Ibid.*, **13,** 107.
15. Ricono, M. (1911): *Ibid.*, **9,** 215.
16. Knobel, J. B. (1916): *Ibid.*, **14,** 151.
17. Cairns, P. T. (1911): *Ibid.*, **9,** 67.
18. Walker, P. H. (1911): *Ibid.*, **9,** 182.
19. Hudson, E. H. (1937): Trans. Roy. Soc. Trop. Med. Hyg., **31,** 9.
20. McArthur, D. C. (1922): Amer. J. Syph., **7,** 569.
21. Sax, S. (1952): S. Afr. Med. J., **26,** 1037.
22. Mitchell, J. A. (1917): S. Afr. Med. Rec., **15,** 186.
23. Kark, S. L. (1949): S. Afr. Med. J., **23,** 77.
24. Leipoldt, C. L. (1920): Med. J. S. Afr., **16,** 25.
25. Pijper, A. (1921): S. Afr. Med. Rec., **19,** 302.
26. Schultz, H. J. E. (1921): Med. J. S. Afr., **21,** 209. Quoted by Anning.[28]
27. A. R. S. Afr. Inst. Med. Res. (1927): P. 56.
28. Anning, C. C. P. (1948): Leech, **19,** 9.
29. Kark, S. L. and le Riche, H. (1944): Manpower, **3,** 1.
30. Purcell, F. W. F. (1940): S. Afr. Med. J., **14,** 453.
31. Ann. Med. Rep. Bechuanaland Protectorate Govt. (1946).
32. Ricono, M. (1916): S. Afr. Med. Rec., **14,** 83.
33. Garrow, A. (1915): *Ibid.*, **13,** 89.
34. Jones, L. G. G. (1953): Brit. J. Vener. Dis., **29,** 104.
35. Hill-Aitkin, C. J. (1908): Transv. Med. J., **3,** 310.
36. Marshall, J. and Wilson, G. A. (1949): S. Afr. Med. J., **23,** 783.
37. Mitchell, J. A. and Robertson, G. W. (1915): S. Afr. Med. Rec., **13,** 28.
38. Murray, J. F. *et al.* (1957): S. Afr. Med. J., **31,** 657.
39. Grin, E. I. (1952): Bull. Wld. Hlth. Org., **7,** 1.
40. Guthe, T. and Willcox, R. R. (1954): Chron. Wld. Hlth. Org., **8,** 37.
41. Murray, J. F. *et al.* (1957): Bull. Wld. Hlth. Org., **15,** 975.
42. Willcox, R. R. (1951): S. Afr. Med. J., **25,** 501.
43. Taylor, W. N. (1954): *Ibid.*, **28,** 176.
44. Hackett, C. J. (1953): 1*st International Symposium on Yaws Control*, Wld. Hlth. Org., p. 158.
45. Bensusan, A. D. (1952): S. Afr. Med. J., **26**, 389.
46. Sachs, S. B. (1953): Personal communication.

RENAL STONE

A STUDY OF 520 PATIENTS WITH SPECIAL REFERENCE TO THE PATTERN OF RECURRENCE

M. MODLIN, M.B., CH.B. (CAPE TOWN), F.R.C.S. (ENG.)

Cape Town

This study has been carried out on a group of 520 patients with renal stone. The cases were seen in the Department of Urology, Leeds, during a period of 2 years 1955-56. No selection was made in relation to duration of attendance. All the cases were seen regularly for follow-up after their first attendance.

The first impression gained on studying these cases was that they could be divided into 2 main groups viz:

1. *Cases presenting with their first renal stone.* The number of cases falling into this group was 419 (80%). Of these, 365 cases (87%) presented with a unilateral stone and 54 cases (13%) presented with bilateral stone.

2. *Cases presenting as recurrent renal stone.* The cases in this group numbered 101 (20%).

The term 'renal stone' is used in this paper to indicate either a single calculus or multiple calculi, unilateral or bilateral. The term 'recurrence' is used to indicate the development—isolated or repeated—of further stone, after removal or spontaneous passage of a previous stone, or in the presence of a previous stone.

RENAL CALCULOUS DISEASE

The term renal calculous disease is here used to denote the presence of renal stone as the clinical manifestation of a disease process affecting the renal tissue. Certain cases have an established etiological agent, such as hyperparathyroidism, primary renal acidosis, cystinuria, or recumbency. The vast majority of cases, however, have no proven etiological agent, although in some there are associated conditions suspected as etiological and as yet under investigation. For the group as a whole the term 'renal calculous disease' is suggested until more precise knowledge of the various etiological agents is available. Renal calculous disease may present clinically as a unilateral or a bilateral condition.

Unilateral Calculous Disease

Here the disease process appears to affect only one kidney. In this series there were 399 cases (76%) in which the disease has remained unilateral up to the present date. This group can be further divided into:

1. *Cases with no recurrence.* There were 342 such cases (86%), of which 153 (45%) presented as a ureteric stone.
2. *Cases with ipsilateral recurrence*, numbering 57 (14%).

Bilateral Calculous Disease

Clinically there are two distinct groups of cases in which both kidneys are affected by the disease process: (1) Cases presenting initially with bilateral stone, and (2) cases where both kidneys become affected at an interval of time, i.e. initially unilateral cases developing a contralateral recurrence. Both must be taken into account in assessing the incidence of bilateral calculous disease.

1. *Cases presenting initially with bilateral stone.* There were 54 such cases among the 419 seen with their first stone (13%). Among those which had recurred when first seen, 10 cases were known to be bilateral originally. A survey

TABLE I. INCIDENCE OF BILATERAL STONE

Year	*Series*	*Incidence %*
1917..	Kummel	16·0
1918..	Braasch	12·3
1924..	Chute	18·0
1925..	Thomas	12·0
1934..	Winsbury-White	13·0
1938..	Andres	16·4
1939..	Parmenter	8·0
1956..	Modlin	13·0

of the literature reporting the incidence of bilateral stone is presented in Table I. The reported incidence has been fairly constant.

2. *Cases with contralateral recurrence*, i.e. those where the second kidney became involved at a later stage. In the series of 520 cases there were 57 such cases.

Bilateral renal involvement by stone at some stage thus occurred in a total of 121 cases i.e. 24%, as compared with 13% presenting initially with bilateral stone. Correctly assessed in this way, there is thus a higher incidence of bilateral renal involvement than is generally stated.

PATTERNS OF RECURRENCE

Total Recurrence Rate

In the whole series there have been 48 cases that have developed recurrence since first attending the department, i.e. a 9% recurrence rate. This figure is not related to time; it is the figure at the time of studying the series. A survey

TABLE II. INCIDENCE OF RECURRENCE OF RENAL STONE

Year	*Series*	*Recurrence Rate %*
1924..	Chute	32·0
1924..	Braasch and Foulds	10·79
1925..	Thomas	33·0
1931..	Herbst	15·0
1933..	Higgins	16·4
1940..	Twinem	8·0
1956..	Modlin	9·0

of recurrence rates as reported by various observers is given in Table II. It will be seen that the last two figures in the table almost correspond. As Twinem's survey[1] was carried out in the USA, the recurrence rate would not seem to be influenced geographically, nor has it altered in the past decade.

Recurrence in cases that presented with their first renal stone

In this group of 419 cases the number of cases that have developed recurrence while under observation has been 32 (8%). The following is an analysis of the site of recurrence:

Cases developing ipsilateral recurrence ..	14
Cases developing contralateral recurrence ..	9
Cases of bilateral stone developing recurrence..	9

Recurrence in cases that presented as recurrent renal stone

There were 101 cases in this group. The following is an analysis of their recurrence pattern up to the time of presenting at the department:

Cases with ipsilateral recurrence only	49
Cases with contralateral recurrence	28
Cases presenting with bilateral stone	24

The last group of 24 was further analysed as follows to determine what was the pattern of recurrence that had resulted in their presenting with bilateral stone:

Ten cases had in fact started as bilateral renal stone and had subsequently developed recurrence, with which they presented still as bilateral stone. The remaining 14 cases were originally unilateral. Of these 12 had become bilateral by developing bilateral recurrence (i.e. ipsilateral and contralateral recurrence), and the remaining 2 had become bilateral as the result of contralateral recurrence. Thus in all 14 there was contralateral recurrence.

Of the 49 cases in this group seen with ipsilateral recurrence only, 6 developed contralateral recurrence while under observation; thus the number of cases in this group remaining as pure ipsilateral recurrence was 43.

Reference to this analysis will be made again later.

Recurrence in this group while under observation. In this group of 101 patients who presented with recurrence, 16

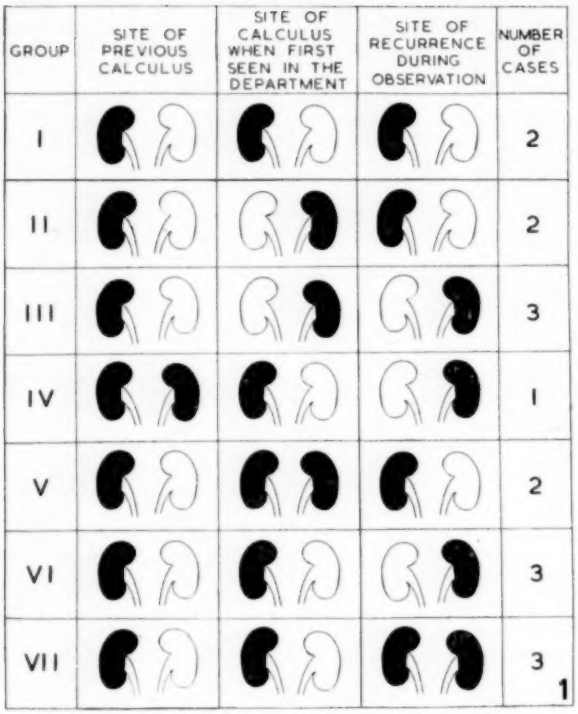


Fig. 1. Patterns of Recurrence. The black kidney denotes the affected side (see Table III).

developed a further recurrence (16%). This figure is double the recurrence rate in patients with first stone. The chance of recurrence after subsequent stone is thus twice as great as the chance of recurrence after first stone. An analysis of the recurrence history in these 16 cases was made by means of a series of diagrams (Fig. 1). The descriptive details are given in Table III and reference to Fig. 1 will assist in the interpretation

TABLE III. FURTHER RECURRENCES IN CASES FIRST SEEN AS RECURRENCES

Group	*Description*	*No. of Cases*
Group I	Ipsilateral recurrence in an ipsilateral recurrer	2
Group II	Contralateral recurrence in a contralateral recurrer	2
Group III	Ipsilateral recurrence in a contralateral recurrer	3
Group IV	Contralateral recurrence in an ipsilateral and contralateral recurrer	1
Group V	Ipsilateral recurrence in a bilateral recurrer	2
Group VI	Contralateral recurrence in an ipsilateral recurrer	3
Group VII	Bilateral recurrence in an ipsilateral recurrer	3
	Total	16

of the terms used. The series of diagrams clearly demonstrates the various patterns of recurrence that may occur and enables each recurrence to be correctly interpreted. Six cases of true contralateral recurrence in this group were detected in this way.

The patterns illustrated in Fig. 1 probably occur throughout renal-stone recurrence and these 16 cases provided an excellent opportunity of studying this feature. Of importance is the demonstration that there may at any time in the natural history of the disease process be contralateral recurrence (groups VI and VII, Fig. 1).

Contralateral Recurrence

The recurrences in the various groups of cases have been analysed in the preceding paragraphs. By means of these analyses it was possible to pick out all the cases with contralateral recurrence and these have been assembled in the manner shown in Table IV. In the whole series there were 57 cases with contralateral recurrence.

The total number of cases in the series with a recurrence was 133, made up of 101 cases which had already recurred when first seen and 32 cases, seen initially with their first stone, which developed a recurrence while under observation. In the group of 101, 10 started as bilateral stone and in the group of 32, 9 were initially bilateral. Excluding these 19

TABLE IV. CONTRALATERAL RECURRENCES

Group	*Description of Cases*	*No. of Cases*
I	Among those seen with their first stone	9
II	Among recurrers when first seen:	
	Unilateral stone cases which were contralateral recurrences when first seen	28
	Cases seen as bilateral stone; as a result of a bilateral recurrence in a unilateral stone (i.e. ipsilateral and contralateral recurrence)	12
	Cases seen as bilateral; as a result of a contralateral recurrence only ..	2
III	Among recurrences in cases which were recurrers when first seen:	
	Contralateral recurrence in a case first seen as an ipsilateral recurrer (Group VI, Table III)	3
	Bilateral recurrence in a case first seen as an ipsilateral recurrer (Group VII, Table III)	3
	Total	57

cases of initially bilateral stone, there remain 114 cases of unilateral stone with recurrence. Of these 114 cases, as shown in Table IV, 57 were cases of contralateral recurrence i.e. 50%. Thus the chance of stone recurrence in the kidney not affected is as great as the chance of recurrence in the previously affected kidney. This is of considerable importance in studying the etiology of renal calculous disease and in the prevention of recurrence by present methods.

For the purpose of comparative study these 57 cases were divided into 2 groups:

1. The cases that had developed contralateral recurrence after investigation and treatment elsewhere. They numbered 42 (group II, Table IV).

2. The cases that developed contralateral recurrence after investigation and treatment in the department. They numbered 15 (groups I and III, Table IV).

Dealing only with unilateral calculous disease, in the first group there was a total of 91 cases with recurrence, the 42 cases with contralateral recurrence representing 46% of this total. In the second group there was a total of 37

cases with recurrence, the 15 cases with a contralateral recurrence representing 40% of this total. The small drop in percentage may possibly be accounted for by the elimination, in a specialized department, of the known etiological agents, but the difference is so small as to confirm the great extent to which the nature of the disease remains unknown.

Ipsilateral Recurrence in unilateral calculous disease

The number of cases of ipsilateral recurrence in unilateral calculous disease in this series was 57. For the purpose of comparison these were divided into 2 groups depending on whether they were treated for their previous stone elsewhere or in this unit:

1. There were 43 cases with ipsilateral recurrence after treatment elsewhere (when first seen there were 49 cases, but 6 later developed contralateral recurrence while under our observation). This represents 47% of the total of 91 cases of unilateral stone with recurrence in this group.

2. There were 14 cases that developed ipsilateral recurrence after treatment on this unit. This represents 60% of the total of 23 unilateral stone cases with recurrence in this group. As the first group have had renal calculous disease for a longer period, the figure or 47% is probably more nearly correct. It can be confidently expected that in the second group more cases will ultimately develop a contralateral recurrence as the natural history of the disease process proceeds unchecked (Groups VI and VII, Fig. 1). The figure of 60% is thus an interim one and will decrease in time with an increase in contralateral recurrence rate.

Recurrence in cases presenting with bilateral stone

There were 54 cases with bilateral stone among the 419 cases seen with their first stone. Of these 54 cases, 9 have had recurrence while under observation, i.e. 17%. This is almost double the total recurrence rate.

ETIOLOGY

Certain factors are dealt with in Table V.

Sex

In the total series the ratio of male to female is 2:1. The ratio is the same in unilateral first stone cases without recurrence and is about 3 : 1 in cases with ipsilateral recurrence. In cases with contralateral recurrence there is a decided increase in the proportion of females affected, and in bilateral stone the sexes were almost equally affected. Thus it would seem that whatever factor operates in affecting both kidneys does so with increasing frequency in females, when compared with unilateral calculous disease, and that bilateral calculous disease affects the sexes almost equally. In searching for causes of bilateral calculous disease, factors related to sex *per se* can apparently be eliminated.

TABLE V. INCIDENCE OF FACTORS IN THE VARIOUS GROUPS

	Total Series	*Unilateral Stone and no Recurrence*	*Ipsilateral Recurrers*	*Unilateral Calculous Disease*	*Contralateral Recurrers*	*Bilateral Stone*	*Bilateral Calculous Disease*
No. of Cases ..	520	342	57	399	57	64	121
Male	65%	66%	74%	70%	58%	53%	55%
Female	35%	34%	26%	30%	42%	47%	45%
Family History ..	10%	10%	9%	10%	10%	16%	13%
Renal Infection ..	10%	9%	7%	8%	12%	11%	11%

Family History

A history of stone in father, mother, grandparents, brothers, sisters or children is surprisingly frequent in all groups. The figure is fairly constant throughout the various groups (Table V).

Further investigation is required to see whether there is a genetic or an environmental basis for this. It should be considered along with reports of geographical 'stone forming areas'.

Renal Infection

In the investigation of renal infection as an etiological agent, careful evaluation was made of the history and definite proof was demanded of renal infection prior to stone formation. Infection at the time of examination, in the presence of or following stone, was not in itself regarded as sufficient evidence. Evaluated in this manner, renal infection was found fairly consistently throughout the groups (Table V). It does not occur with significantly greater frequency in the recurrences, and in fact in the ipsilateral recurrences it operates less frequently, which is contrary to what one would expect if it were a significant etiological factor.

Hypercalciuria

Hypercalciuria has been said by some investigators to play a part in renal stone formation (Flocks[2]). In this series the total number of cases with a urinary calcium output, on a normal diet, of over 350 mg. per 24 hours was 50 (excluding cases of hyperparathyroidism). Of these, 45 were males and 5 were females, a ratio of male to female of 9 : 1. In a recent review by Hodgkinson[3] of the urinary calcium output in a group of 320 cases of renal stone the ratio of male to female among the hypercalciurics (i.e. with an output of over 350 mg. of calcium in 24 hours on a normal diet) was 4 : 1. The ratio probably lies somewhere between these two sets of figures, but what seems certain is that there is a marked preponderance of males. As can be seen in Table V, as we come to examine the cases with bilateral calculi and contralateral recurrences (i.e. the cases of bilateral calculous disease) the ratio of male to female is altered so that the number of females increases and approximates to the number of males. If hypercalciuria were causal or contributory in renal stone formation, one would expect it to act equally in relation to both kidneys and the cases with bilateral renal involvement should be predominantly male. In bilateral renal calculous disease, however, the sexes are equally affected, thus making it difficult to substantiate a claim for hypercalciuria *per se* as an etiological factor.

CONCLUSIONS

The total recurrence rate of renal stone in this series was 9%. This rate has not decreased in the last decade and does not appear to be influenced by geographical factors.

The recurrence rate after first stone was 8% and recurrence rate after subsequent stones was 16%. Thus the chance of a recurrence after subsequent stones is twice as great as the chance of a recurrence after a first stone.

The contralateral recurrence rate is 50% of the recurrence rate, as compared with figures ranging from 11% to 15%

previously reported. Thus the chance of a recurrence in cases presenting with unilateral stone is the same in both kidneys.

The incidence of bilateral stone when first seen was 13%. The incidence of bilateral renal involvement by stone at any stage, however, was 24%.

The recurrence rate in cases presenting initially with unilateral stone was 6%.

The recurrence rate in cases presenting initially with bilateral stone was 17%, which is 3 times the rate of recurrence in unilateral first stone and double the total recurrence rate.

It would appear that abnormal changes occur in renal tissue, as a result of which there may be stone formation. In most instances the causative factor and its associated manifestations are unknown, renal stone being the only manifestation. Little is known regarding either the precise nature of the renal changes or the exact mechanism of stone formation.

True bilateral renal involvement by stone, as assessed above, occurred in 24% of patients in this series. It has also been demonstrated that when there is stone recurrence it is as likely to be in the unaffected as in the previously affected kidney; that it to say, 50% of recurrences are contralateral. These two features suggest that the abnormal changes in renal tissue are probably originally bilateral. The changes may exist temporarily, which is suggested by the fact that no recurrence of stone takes place in some cases; or intermittently or continuously as is suggested by the various patterns and rates of recurrence.

In bilateral calculous disease the sexes are equally affected and if bilateral involvement by stone could be regarded as an end state in the natural history of the abnormal renal changes, then sex-determined factors do not appear to play a part in etiology. The role of infection in etiology, if correctly assessed, would seem to be of less significance than previously thought. Hypercalciuria *per se* does not appear to be an etiological factor. There does however, appear to be a family history in an appreciable number of cases and this requires further investigation.

SUMMARY

A study has been made of 520 patients with renal stone.

True bilateral involvement by stone was found to occur in 24% of these patients.

The various patterns of recurrence have been worked out. A most striking feature is a contralateral recurrence rate of 50%.

Certain conclusions have been drawn regarding the abnormal renal changes occurring in patients with renal stone.

An attempt has been made to evaluate the role in etiology of sex, family history, renal infection and hypercalciuria.

The term renal calculous disease is suggested for a group of conditions having renal stone as a clinical manifestation.

Acknowledgement is made to Prof. L. N. Pyrah and Mr. F. P. Raper, both of the Deparment of Urology, Leeds, for access to their patients and case notes.

REFERENCES

1. Twinem, F. P. (1940): Surg. Clin. N. Amer., **20,** 299.
2. Flocks, R. H. (1940): J. Urol., **43,** 214.
3. Hodgkinson, A. (1956): Dept. of Urology, Leeds, Unpublished data.

LIVER FUNCTION TESTS IN PRIMARY CARCINOMA OF THE LIVER IN THE SOUTH AFRICAN BANTU

I. BERSOHN, B.SC., M.B., B.CH. (RAND)

Head of the Liver Function Unit, South African Institute for Medical Research, Johannesburg

Primary carcinoma of the liver is a rare disease amongst Western population groups, irrespective of whether they live in Africa, America or Europe, but is a relatively common condition amongst the Bantu races of Africa and in certain Oriental races, where according to Berman[1] the incidence may be 40 times as frequent as in Western people. Primary carcinoma of the liver is the commonest form of malignancy encountered in Bantu males.[1]

It follows therefore that a clinical diagnosis is rarely made in the European, but even amongst the Bantu, where a clinical diagnosis of primary liver carcinoma is more readily made, difficulty in establishing such a diagnosis still exists, since primary carcinoma of the liver must be distinguished from many other conditions which give rise to hepatic enlargement.

I have carried out a large series of 'liver function tests' on suspected cases of primary carcinoma of the liver, with the hope that by careful selection of biochemical criteria it might be possible to establish a diagnosis of hepatoma more confidently, without resorting to liver biopsy. And here it must be borne in mind that even a liver aspiration biopsy may not be conclusive, since it is obvious that a small fragment of liver tissue may fail to reveal the malignant growth.

REVIEW OF LITERATURE

A review of the literature on the value of liver function tests in the diagnosis of primary carcinoma of the liver reflects conflicting opinions. Thus, Berman[1] in discussing laboratory aids in the diagnosis of primary carcinoma of the liver states that most liver function tests devised thus far are of doubtful value. 'I have seen', he says, 'many cases where the liver was practically replaced by carcinoma, and all liver function tests proved normal.' He attaches some importance to the van den Bergh test, especially as a means of detecting latent jaundice.

Stein[2] found the Takata-Ara reaction useful in differentiating between intra-hepatic and extra-hepatic carcinoma. In 6 cases of primary liver cancer he found the Takata reaction positive in 5, and the negative reaction occurred in spite of massive infiltration of almost all the

liver tissue. In 4 other anicteric cases of primary cancer of the liver the Takata reaction was positive in all.

Spellberg[3] states 'that liver function tests in primary carcinoma of the liver are variable, and depend to a great extent on the presence of an underlying cirrhosis'. If there is a marked derangement of the 'liver profile' the presence of cirrhosis is likely. He does state however that 2 tests are likely to be positive, in both primary and secondary malignant liver disease, viz. the bromsulphalein dye retention test and an elevated serum alkaline-phosphatase level.

In Lichtman's opinion[4] the bilirubin content is usually negative, the cephalin cholesterol test is strongly positive in primary carcinoma of the liver and negative in secondary carcinoma, and the thymol turbidity reaction is more uniformly negative in hepatic cancer. He states, too, that the alkaline phosphatase level may be normal in primary carcinomata which develop in cirrhotic livers.

Holley and Pierson[5] found that liver function tests as a rule were disappointing as a method of diagnosis of primary carcinoma of the liver. They state that damage must be extensive before any appreciable change could be detected in the function tests.

Spatt and Grayzel[6] state that the most consistent abnormal liver function tests in primary liver cancer were a raised icteric index, a raised alkaline phosphatase level and an abnormal bromsulphalein dye retention. The serum protein and serum cholesterol and the cephalin flocculation tests were not significant in the diagnosis.

Ricketts[7] discusses certain liver function tests in 2 cases of primary hepatoma of the liver. The one case was anicteric and had a slow-growing hepatic tumour of 8 years standing. The only abnormal tests were an elevated alkaline phosphatase test and abnormal bromsulphalein dye retention. The other cases was in a jaundiced Chinese subject, who had a very slightly elevated alkaline phosphatase level (13·5 units) and a slightly elevated serum-cholesterol level. All other liver function tests, including an albumin-globulin ratio, were normal in these 2 subjects.

Most of the authorities cited above base their data on European subjects and, as the biochemical pattern of the Bantu, especially that of serum protein and the commonly used flocculation and turbidity tests differ so markedly from that of the European, I decided to investigate whether, by carrying out a so-called 'battery of liver function tests', it would be possible to show a specific type of pattern in primary malignant disease of the liver, bearing in mind the connection between cirrhosis and primary carcinoma of the liver, and whether the coexistence of these two disease processes would not confuse the biochemical pattern.

MATERIAL AND METHODS

The investigation covered 37 cases of primary carcinoma of the liver in the African male Bantu. The diagnosis of all these cases was proved either by biopsy or by autopsy or by both. A 'battery of liver function tests' was carried out on serum from these cases on their admission to hospital. The biochemical tests and techniques used were as follows:

1. Thymol turbidity test (MacLagan)[8]
2. Thymol flocculation test (Neefe and Rheinhold)[9]
3. Colloidal-red test (Ducci)[10]
4. Cephalin-cholesterol flocculation test (Hanger)[11]
5. 'Takata-Ara' reaction (Ucko)[12]
6. Zinc-sulphate turbidity (Kunkel)[13]
7. Total lipid (Kunkel *et al.*)[14]
8. Alkaline phosphatase (King and Armstrong)[15]
9. Bilirubin, (*a*) direct, (*b*) total (Malloy and Evelyn)[16]
10. Pseudo-cholinesterase (Michel)[17]
11. Mucoprotein (Simkin *et al.*)[18]
12. Total cholesterol (Kaye)[19]
13. Free cholesterol (Kaye)[19]
14. Serum electrophoretic pattern
15. Bromsulphalein test (5 mg. of dye per kg. of body weight was injected intravenously and the percentage of dye retained at the end of 45 minutes was estimated). This test was performed in only 7 and 4 cases in the malignant and cirrhotic groups respectively.

The electrophoretic protein-analyses were carried out on the Antweiler micro-electrophoretic apparatus, with the use of a modified Michaelis buffer solution (pH 8.6).

TABLE I. LIVER FUNCTION TESTS IN BANTU SUBJECTS WITH PRIMARY CARCINOMA OF THE LIVER AND WITH CIRRHOSIS OF THE LIVER, AND IN NORMAL BECHUANA AND EUROPEAN SUBJECTS

	Primary carcinoma of the Liver, Bantu (37 cases)	*Cirrhosis of Liver Bantu (20 cases)*	*Normal Bechuana African (50 cases)*	*Normal European Adult*
Thymol Turbidity Test (units) ..	6·5	5	4	0-2
Thymol Flocculation Test ..	1·3+	2·5+	2·2+	neg.
Colloidal-red Test	2·7+	3·5+	3·6+	+−neg.
Cephalin-Cholesterol Test ..	2·3+	3+	2+	neg.
Takata Ara (Ucko)	2·1+	2·5+	1·5+	neg.
Zinc-sulphate Turbidity Test (units)	25	35	22	12·5
Total Lipids (mg/100 ml.) ..	541	450	490	600
Alkaline Phosphatase (K.A. units)	31·4	12·3	7·5	8
Bilirubin Total (mg/100 ml.) ..	3·8	0·9	0·5	up to 1·2
Cholinesterase (△p H/hr.) ..	0·325	0·430	0·630	0·710
Mucoprotein (mg/100 ml.) * ..	205	70	110	80
Cholesterol Total (mg/100 ml.) ..	240	135	150	230
Cholesterol Esters (mg/100 ml.) ..	144	81	110	160
% Esters to Total	60	60	73	70
Total Protein (g/100 ml)† ..	7·3	7·8	7·7	7·1
% Albumin	29·2	33·0	42·7	55·0
% $Alpha_1$ globulin	3·9	3·0	3·8	2·0
% $Alpha_2$ globulin	13·1	7·2	9·4	6·5
% Beta globulin	16·9	12·2	12·6	15·5
% $Gamma_1$ globulin	5·5	6·2	5·5	4·5
% $Gamma_2$ globulin	31·4	38·4	26·0	16·5

* Performed in 10 cirrhotic cases and 21 cases of carcinoma of the liver.
† Performed in 10 cirrhotic cases and 21 cases of carcinoma of the liver.
The bromsulphalein tests carried out on the 7 carcinoma and 4 cirrhotic cases are not included in this table (see text).

RESULTS AND COMMENTS

Table I shows the results of the liver function tests (mean values) carried out on the 37 cases of primary carcinoma of the liver. Mean results of similar tests carried out on a group of 50 'normal' Bechuana male subjects on their arrival in Johannesburg, on a group of 20 Bantu cirrhotic patients (proved by liver biopsy) and on a group of 100 healthy European adult subjects are also shown for comparison.

From the table, it is obvious that results on the so-called 'normal' Bantu differ markedly from his normal European counterpart.

Comments on Results

Turbidity and Flocculation Tests. The thymol turbidity test was slightly higher in the malignant than in the cirrhotic group, but probably not significantly so. There appears to be a disassociation between the thymol turbidity and the thymol flocculation tests in the malignant group. Usually, these two tests parallel each other closely, but in our malignant group there were 13 cases where the thymol turbidity test was high (as high as 15 units—average 8 units) with negative flocculation tests. The reverse is often found in residual hepatitis, where one may find a positive thymol flocculation test with a normal turbidity result, but our finding in malignant

liver disease is unusual. We have occasionally encountered similar findings in liver damage due to malignant extra-hepatic obstruction. Is there a substance in malignant sera which inhibits the thymol flocculation test? Whereas only 6 cases had a normal thymol turbidity test (2·5 units and lower), 25 cases showed normal thymol flocculation tests. The mean values for the colloidal-red, the cephalin-cholesterol flocculation tests and the Takata reaction did not differ significantly in the 2 groups of patients. In 5 cases of liver cancer the Takata reaction was negative.

The zinc-sulphate turbidity test was lower in the carcinoma than in the cirrhotic group, whilst the reverse applied to the serum-lipid level.

Alkaline Phosphatase. The mean level was definitely higher in the carcinoma group, 31·4 units, as compared with 12·3 units in the cirrhotic subjects. In the liver-cancer group, a normal level of 8 units or less was found in only 1 case, and in only 5 cases was the serum level below 13 units. In 22 cases a definite elevation of the phosphatase level was shown, with a low serum-bilirubin content (e.g. bilirubin 0·4 mg. per 100 ml., alkaline phosphatase 45 units).

Bilirubin. The mean serum-bilirubin level was 3·8 mg. per 100 ml. in the primary-carcinoma group as opposed to a mean level of 0·9 mg. per 100 ml. in the cirrhotic group. Of the carcinoma patients 17 were anicteric and 19 had a bilirubinaemia, which in the majority of patients was slight. Only 5 patients showed a bilirubin level of 10 mg. per 100 ml. or higher.

Cholinesterase. The level of serum pseudo-cholinesterase was slightly lower in the carcinoma group than in the cirrhotic group. Only one patient gave a normal result in the former group and one patient had a level of only 4% (100% = △ pH, 0·710).

Mucoprotein. The mucoprotein serum-content was significantly higher in the malignant than in the cirrhotic cases (205 mg. per 100 ml. as against 70 mg. per 100 ml.) Only one case of primary carcinoma of the liver had a normal mucoprotein level (75 mg. per 100 ml.)

Cholesterol. The cholesterol level in the hepatoma group was increased when compared with the cirrhotic group (240 mg. per 100 ml. as opposed to 135 mg. per 100 ml.) The cholesterol level in the malignant group approximated to the level found in healthy European subjects. The percentage of cholesterol esters to total cholesterol was the same in the malignant and cirrhotic groups, both showing a slightly decreased percentage of esterfied cholesterol.

Protein. The total protein serum-content was virtually the same in the 2 groups. Significant features in the electrophoretic protein-analyses in the hepatoma group were an increased percentage of the alpha$_2$-globulin fraction (in only one case was this level below 7% and in one case as high as 31·8%) and an increased percentage of the beta-globulin fraction (in only one case was this fraction below 12% and in one case as high as 23·2%). The gamma-globulin level in the malignant group was intermediate between that found in the cirrhotic patients and in the 'normal' Bantu. The albumin serum-content showed a slight reduction in the malignant group when compared with the cirrhotic group.

Bromsulphalein Dye Retention. As stated above, this test was only carried out on 7 cases of carcinoma of the liver and on 4 cases of cirrhosis of the liver. Abnormal dye retention (more than 5%) was found in each of the 11 cases. The highest level of dye retention in the malignant groups was 53% and the lowest level was 6·0%.

DISCUSSION

The diagnostic biochemical features of primary carcinoma of the liver appear to be the following:

1. A disassociation between the thymol turbidity and flocculation tests.
2. A disassociation between the degree of bilirubinaemia and the serum alkaline-phosphatase level, expecially the presence of a raised phosphatase level in the anicteric patient.
3. A raised serum-mucoprotein level and
4. A definite elevation of the alpha$_2$- and beta-globulin serum-fractions.

The disassociation between the thymol turbidity and flocculation tests is referred to above. The disparity between the degree of bilirubinaemia and the high phosphatase levels was a striking feature in our series of cases. Shay and Siplet[20] suggest that this may reflect the sensitivity of the alkaline-phosphatase test to obstruction. The growth may obstruct enough bile canaliculi to cause an elevation of the phosphatase, but not enough to cause an increase in the serum bilirubin. Another hypothesis they put forward was that metastasis to the hilus nodes caused compression of the common duct sufficient to raise the pressure in the biliary tree to increase the blood-phosphatase level but not the serum-bilirubin level.

Gutman *et al*[21] suggest that a rise in phosphatase levels in the absence of jaundice, may be dependent upon the excretion of bile in the urine and the impermeability of the human kidney to phosphatase excretion.

Bilirubinaemia was not a prominent feature in our series of cases. Of 36 cases 17 were anicteric, and in those showing bilirubinaemia the degree of jaundice was usually slight.

Holley and Pierson[5] stated that 4 out of 5 of their patients with primary carcinoma of the liver were jaundiced either at the time of admission or subsequently and that, though the jaundice was not intense, it was a fairly constant feature.

Likewise, Spatt and Grayzel[6] found a raised icteric index in 9 cases of primary carcinoma of the liver (average 84·1 units) and in only 2 cases was this index below 10 units. The icteric index in their group was high fairly consistently.

I have used the criteria of a raised alkaline-phosphatase level in the absence of jaundice as a useful aid in the diagnosis of malignancy, not necessarily confined to the liver. I have previously found this disassociation of the alkaline-phosphatase level and degree of bilirubinaemia in space-occupying tumours of the liver such as hydatid cyst, tuberculoma, amoebic abscess etc.

The level of serum mucoprotein was found by Greenspan *et al.*[22] to be elevated in 95% of patients with clinically evident enlargement of the liver due to neoplastic infiltration. Mucoprotein is a glucoprotein complex, probably related to changes in the alpha globulins, which changes are not detected when electrophoretic analyses are carried out at an alkaline pH but only when performed at an acid pH.

The concentration of mucoprotein in the serum appears to represent the resultant of both intra-hepatic and extra-hepatic processes. Greenspan *et al.*[22] found a reduced mucoprotein level in infectious hepatitis and portal cirrhosis and a raised level in obstructive, inflammatory and neoplastic

diseases of the biliary system. I have found that, unless the cirrhosis or hepatitis is severe, it is more usual to find a low normal rather than a reduced mucoprotein level, but have not encountered elevated levels. In primary carcinoma of the liver, there is usually an accompanying cirrhosis, and the raised levels found in this series of malignant disease of the liver shows that the malignant process more than counteracts the damage to the parenchymal liver tissue. *In my opinion, the mucoprotein test is one of the best in the differential diagnosis between cirrhosis and malignant disease of the liver.*

A high cholesterol serum level favours a diagnosis of primary carcinoma of the liver rather than cirrhosis, but the range of serum-cholesterol levels was found to be very wide (86-580 mg. per 100 ml.) I therefore think that no importance can be attached to the serum-cholesterol level.

The low serum albumin probably reflects parenchymal liver impairment in both groups. Alpha-globulin levels are usually increased by inflammation and/or tissue destruction. Two competitive factors account for the wide range in distribution of the alpha globulins: the tendency for a rise with a drop in albumin and the tendency for a fall in liver-cell damage. It appears that the rise in the alpha$_2$-globulin fraction in the carcinoma group reflects evidence of tissue destruction.

The beta-globulin fraction is concerned in the transport of lipids, and is elevated in most hepatobiliary diseases, especially those in which there is a concomitant rise in the serum lipids. The increased cholesterol and lipid levels in the carcinoma patients probably account for the raised beta-globulin fraction found in this group.

SUMMARY

1. 37 cases of proved primary carcinoma of the liver were subjected to a 'battery of liver function tests'. These results and results of similar tests performed on normal European and normal Bantu subjects and on patients suffering from cirrhosis of the liver are presented.

2. The following are diagnostic features in differentiating malignant liver disease from cirrhosis of the liver:

(i) A disassociation between the thymol turbidity and flocculation tests.

(ii) A disassociation between the serum bilirubin and alkaline phosphatase levels, especially a raised phosphatase level in the anicteric patient.

(iii) A raised serum-mucoprotein level.

(iv) Elevated alpha$_2$- and beta-globulin fractions.

My thanks are due to Prof. E. H. Cluver, Director, South African Institute for Medical Research, for his interest in this investigation, and to the staff of the Liver Function Unit of the S.A.I.M.R. for technical assistance in carrying out the chemical analyses.

Special thanks are due to Drs. C. Berman of Consolidated Main Reef Mines, E. Hunter of Modder B Mines, and R. Cassell of the S.A.I.M.R., Baragwanath Hospital, who submitted specimens of blood from suspected cases of carcinoma of the liver.

REFERENCES

1. Berman, C. (1951): *Primary Carcinoma of Liver.* London: H. K. Lewis & Co. Ltd.
2. Stein, H. B. (1944): S. Afr. J. Med. Sci., **9,** 41.
3. Spellberg, M. A. (1955): *Diseases of the Liver.* London: Churchill.
4. Lichtman, S. A. (1933): *Diseases of the Liver, Gall Bladder and Bile Ducts,* 3rd ed. London: Henry Kimpton.
5. Holley, H. L. and Pierson, G. (1948): Amer. J. Med., **5,** 561.
6. Spatt, S. D. and Grayzel, D. M. (1948): *Ibid.*, **5,** 570.
7. Ricketts, W. E. (1951): Amer. J. Med. Sci., **221,** 287.
8. MacLagen, N. F. (1944): Brit. J. Exp. Path., **25,** 234.
9. Neefe, J. R. and Rheinhold, J. G. (1946): Gastroenterology, **7,** 393.
10. Ducci, H. (1947): J. Lab. Clin. Med., **32,** 1273.
11. Hanger, F. M. (1939): J. Clin. Invest., **28,** 261.
12. Ucko, H. (1936): Guy's Hosp. Rep., **86,** 166.
13. Kunkel, H. G. (1947): Proc. Soc. Exp. Biol., **66,** 217.
14. Kunkel, H. G., Ahrens, E. H. and Eisenmenger, W. J. (1948): Gastroenterology, **11,** 499.
15. King, E. J. and Armstrong, A. R. (1934): Canad. Med. Assoc. J., **31,** 376.
16. Malloy, H. T. and Evelyn, K. A. (1937): J. Biol. Chem., **119,** 481.
17. Michel, H. O. (1949): J. Lab. Clin. Med., **34,** 1564.
18. Simkin, B., Bergman, H. C. and Prinzmetal, M. (1949): Amer. J. Med., **6,** 734.
19. Kaye, I. A. (1940): J. Lab. Clin. Med., **25,** 996.
20. Shay, H. and Siplet, H. (1948): Amer. J. Med., **4,** 215.
21. Gutman, A. B., Olson, K. B., Gutman, E. B. and Flood, C. A. (1940): J. Clin. Invest., **19,** 129.
22. Greenspan, E. M., Tepper, B., Terry, L. L. and Schoenbach, E. B. (1952): J. Lab. Clin. Med., **39,** 44.

TWO CASES OF SECONDARY CARCINOMA OF BONE WITH PERIOSTEAL REACTION

ROSSALL SEALY, M.A., M.B., CH.B.

and

W. M. ROBERTS, M.B., CH.B.

Departments of Radiotherapeutics and Surgery, Groote Schuur Hospital, Cape Town

Brailsford[1] divides the radiological appearances of secondary carcinoma of bone into 4 types, characterized by (1) erosion of the surface of the bone, (2) multiple islands of cancellous destruction (3) localized areas of denser bone formation, and (4) generalized increase in density of a bone. He associates the last with periosteal reaction, especially in the form of fine radiating spicules. This appearance is well known as a manifestation of secondary carcinoma of bone, although amongst the most unusual. It is sometimes seen as a sign of a secondary bony lesion from neuroblastoma in children[2].

The following two cases are of interest because they represent examples of partially osteoplastic secondary growths from gastric primaries—a well-known but sometimes

forgotten source of such lesions[3]. Both had a resemblance to osteogenic sarcoma in that there was considerable overlying soft-tissue swelling and because they were situated in the humerus. The X-ray appearances were also suggestive of primary bone tumours and, although the age of the patients and the situation in the humerus in case 2 were against this diagnosis, considerable difficulty might have arisen if an indefinite histological report had been returned or had the previous histories not been known.

CASE REPORTS

Case 1

A European male, aged 55, was admitted in May 1955 with a diagnosis of perforated peptic ulcer. Laparotomy showed a perforated gastric carcinoma, which was successfully closed by suture. Seven weeks later the primary was removed at gastrectomy. Histological examination of the primary tumour showed an anaplastic carcinoma (Dr. T. Sacks). The patient presented again in June 1956 complaining of severe pain in the right shoulder for 3 months. There was marked swelling of the whole upper arm, which was tense and tender. A hard fixed epigastric mass and hard mobile right axillary glands were present. The X-ray appearances (Fig. 1) showed irregular cancellous destruction with a few areas of increased density and a fine hair-like periosteal reaction. Biopsy of the node showed (Dr. M. Sacks) the same histological picture as that of the gastric primary, and so did that of the humerus (Fig. 3, Dr. N. Woolf). The growth in the last specimen was somewhat more anaplastic than those in the other two areas examined but clearly of the same origin. Fractionated doses of deep X-ray therapy were followed by complete relief of pain, great reduction in swelling, and restoration of function of the arm. Mid-line dose was 3456 r. (200 kV constant potential; added filter 2 mm. Cu H.V.L. 2·25 mm. Cu F.S.D. 50 cm.). Later an osteolytic area in the dorsal spine developed, and the patient became symptom-free for a while on similar treatment.

Case 2

A Coloured male, aged 53, underwent gastrectomy in February 1956 for carcinoma of the pylorus. Many secondary glands were found at laparotomy and the histology was that of an anaplastic carcinoma (Dr. T. Sacks). He presented again in October 1956, with swelling and pain and a feeling of lameness in the left upper arm. Clinically there was localized thickening in the centre of the lateral aspect of the humerus. There was no evidence of local recurrence of the gastric lesion. X-ray (Fig. 2) showed some sclerosis of the centre of the shaft of the humerus, with overlying spicular formation and partial destruction of the cortex. Biopsy showed the same histology as the gastric primary (Fig. 4, Dr. N. Woolf). The patient discharged himself from hospital before treatment could be given.

Fig. 1. Case 1. X-ray of humerus.
Fig. 2. Case 2. X-ray of humerus.

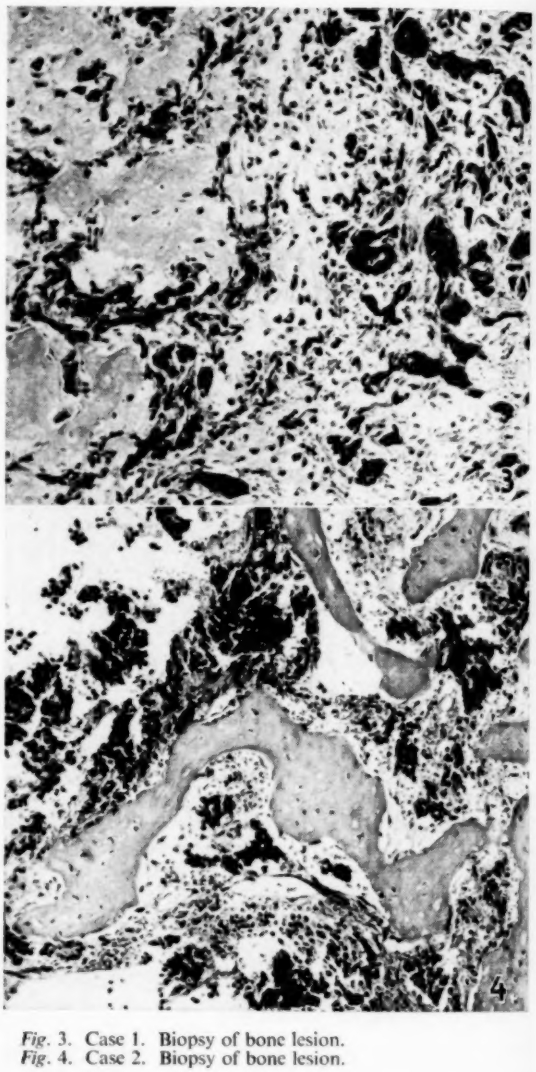


Fig. 3. Case 1. Biopsy of bone lesion.
Fig. 4. Case 2. Biopsy of bone lesion.

The response of the first case to X-ray treatment at once suggested a means of treating the second, although the response of gastric carcinoma to irradiation is very variable. Fairchild and Shorter[4] have treated some primary growths with 250 kV X-rays directly at operation and with supplementary fields later, with some good results, and

radon seeds have also been used for treating primary growths in a few cases with some good effect.[5] It would seem to us that the type of lesions described are at any rate worth a trial of palliative therapy.

SUMMARY

Two cases of metastatic gastric carcinoma are described, both resembling osteogenic sarcoma. The response of one to X-ray therapy is noted and it is pointed out that this may sometimes be a useful palliative agent for gastric carcinoma.

Thanks are due to the Medical Superintendent Dr. N. H. G. Cloete, Dr. J. Muir Grieve and Prof. J. H. Louw for permission to publish the cases and for their advice; to Prof. J. G. Thomson for permission to publish the photomicrographs and to him and his staff for their advice; and to Prof. J. N. Jacobson for permission to publish the X-rays. The photographs of the X-rays were taken by Mr. B. Todt and the photomicrographs by Mr. G. McManus.

REFERENCES

1. Brailsford, J. F. (1953): *Radiology of Bones and Joints*, 5th ed., p. 373. London: Churchill.
2. Caffey, J. (1956): *Pediatric X-ray Diagnosis*, 3rd ed., p. 641. Chicago: Year Book Publishers.
3. Willis, R. A. (1952): *Spread of Tumours in the Human Body*, 2nd ed. London: Butterworth.
4. Fairchild, G. C. and Shorter, A. (1947): Brit. J. Radiol., **20**, 511.
5. Joll, C., Ledlie, R. C. B. *et al.* in Carling, E. R., Windeyer, B. W. and Smithers, D. W., ed. (1955): *British Practice of Radiotherapy*, p. 303. London: Butterworth.

PUERPERAL SEPSIS 1800—1957

JOHN A. STALLWORTHY, F.R.C.S., F.R.C.O.G., F.A.C.S. (HON.)

Regional Director (Obstetrics and Gynaecology, Oxford; 1957 *Guest Professor, University of Cape Town*

There are many people who find the study of history dull. 'It is the wise man who profits by his own mistakes', but it is common sense that he is a wiser man who profits from the mistakes of others. I crave your forbearance, therefore, if occasionally I wander from the strict path of my subject in order to catch a wider view so that we may learn something from the mistakes of the past. The story of puerperal sepsis from 1800 to 1957 is a most exciting one. In terms of the title of my address it must commence with the beginning of the 19th century but I trust you will pardon a very brief prologue so that we may the better see the events of the years in their true focus.

PROLOGUE

Denham and Boer

In the year 1784 the Lying-In Hospital at Vienna was founded and in 1789 Boer was appointed as its director. He worked faithfully and well for 33 years, during which time the institution delivered 65,000 mothers, 850 of whom died—a mortality of 1·3%. Before taking over his appointment Boer had come under the influence in Great Britain of Denham, who 20 years previously, in the year 1768, had stated that childbed fever was contagious and could be transmitted by physicians and by nurses from one mother to another. Based on this belief he taught the principles of cleanliness and patience and maintained that these were the weapons with which to fight the contagion. It is interesting to note that in the year 1770 Levret had questioned whether the forceps used by Smellie might not carry the contagion on the leather with which they were coated. During the years of his work at Vienna Boer had maintained the tradition taught him by Denham and had persistently refused to allow teaching from the cadaver in his maternity institution. It was being progressively more widely accepted that instruction from the cadaver was evidence of scientific progress, and because of his refusal to submit to the pressure brought to bear upon him by the University authorities Boer was ultimately dismissed from his post for insubordination. He was followed by a man called Klein who in the first year of his appointment raised the maternal mortality from 1·3% to 7·8%. He agreed with those who wished for cadaver instruction and employed this method in the hospital. He was followed by Semmelweiss and our story really commences with the years during which Semmelweiss occupied the post of Director of this big institution.

SEMMELWEISS, CEDERSCHORD AND WENDELL HOLMES

Semmelweiss divided the institution into two divisions. In the first of these he delivered 20,042 women with 1,989 deaths—a mortality of 9·9%. In the second division he delivered 17,791 women with 691 deaths a mortality of 3·3%. The essential point of difference between the two divisions was that the first was used for the instruction of medical students whereas in the second the deliveries were conducted by midwives. It follows, therefore, that in the first division were assembled those who were also receiving instruction from the cadaver. There appears to have been no other major point of difference between the work done in the two divisions nor was there evidence of selection of cases for one or other group. It became an established fact, which of course soon became known to the citizens of Vienna, that women whose labours were prolonged were very liable to perish. Scenes of anguish occurred from time to time when women who believed they were being admitted to the second division found that because of shortage of beds or for some other reason they were to enter into the dreaded first division. They would plead at the door of the wards that they should be sent to the second division. Women distended with peritonitis, with bright eyes, high temperatures, rapid pulses and a great fear would lie in the wards protesting that they were not ill because they dreaded receiving the medical assistance which seemed to them to be but a herald of approaching death. It was the custom of the priest as he went around the ward administering the Last Sacrament to toll a little bell, but when nearly one woman in every ten admitted to the first division died as a result of her labour the furtive visits of the priest with his tolling bell had such a detrimental effect on the morale of the patients in the ward, and probably of the staff, that Semmelweiss found it necessary to suggest that the bell was not an essential to the Last Sacrament.

While these terrible happenings were a daily occurrence in the lovely city of Vienna, opinion elsewhere in the world was more progressive. In Stockholm Cederschord in 1839 had stated quite definitely that puerperal fever was carried by nurses and doctors from both the sick and the dead. He therefore ordered that every patient in his wards should have her own sponge and towel and he added chlorine to the water for washing to lessen the danger of transmitting the contagion. The result was that he reduced the epidemics of childbed fever to zero, although sporadic cases still occurred. In the United States of America the poet and essayist, Oliver Wendell Holmes, born at Cambridge, Massachusetts, and a graduate of Harvard, was becoming interested in the problem of puerperal fever. He had studied medicine for 2 years at Paris. His attention was drawn to the tragic case of a physician whose hand was pricked at a post-mortem examination and who subsequently died. Between the time of receiving his injury and his death he had examined a labouring mother, who also died of infection. Holmes considered these tragic events, and in 1843 published a paper on *The Contagiousness of Puerperal Fever*. He proclaimed his belief that this was transmitted from the corpse and from the living when there was associated erysipelas, and laid down 3 clear rules of prophylaxis:

1. That no obstetrician should perform a post-mortem on a patient who had died of puerperal fever.

2. That if an obstetrician was present at such a post-mortem he must thoroughly cleanse himself, change his clothes completely, and not go near a labouring woman for 24 hours.

3. That it was incumbent on obstetricians to avoid all post-mortems but if by any chance or mischance they were present at one of these they should carry out the instructions given in Rule 2.

Two of the leading obstetricians in America at that time were Hodge and Meigs. When Holmes published his paper a battle royal commenced. Hodge retaliated by publishing an article entitled *The Non-Contagiousness of Puerperal Fever*. In this he 'begs students to divest their minds of the dread that they could carry this horrible virus'. Meigs also entered into the fray and in his attack on the teachings of Holmes stated, 'I prefer to attribute deaths to accident or to Providence of which I can form some conception, rather than to a contagion of which I cannot form any idea'. To these attacks Holmes replied, 'No man makes a quarrel with me over the counterpane covering a mother with her newborn infant at her breast,' but while he waved this olive branch in one hand he wielded a scathing pen in the other and now referred to puerperal fever as a 'private pestilence'. In 1855 he published the second edition of his paper, in which he said, 'The time has come when the existence of a private pestilence should no longer be looked on as a misfortune but as a crime'. This was in 1855, and it will be remembered that in Great Britain Denham nearly a hundred years before had laid down his principles of good practice in obstetrics, namely patience and cleanliness.

We must now return to Vienna and the year is 1847. Semmelweiss had a friend who was the Professor of Medical Jurisprudence; his name was Kolletscha. This professor had the misfortune to have his hand pricked by a student during a post-mortem examination and shortly afterwards died. Semmelweiss was present at his post-mortem and as in sorrow he studied the findings, the light dawned. To quote his own words: 'In the excited condition in which I then was, it rushed into my mind with irresistible clearness that the disease from which Kolletscha had died was identical with that from which I had seen so many hundreds of puerpera die.' He asked himself whether the cause of death could have been the injury received by the prick and he decided that this could not be so, for after all so many people had wounds or pricks which caused no difficulty. He then asked could it be as a result of material transmitted from the corpse at the time of the injury, and the answer came to him that it must certainly be 'yes'. The immediate result of this tragic experience was that in May 1847, just 110 years ago, Semmelweiss re-introduced cleanliness into the wards of the Vienna Lying-In Hospital and instituted the use of the chlorine wash. In the first 7 months following these innovations the mortality of the first division was reduced from 11·4% to 3% and by the end of the first year it was down to 1·2%, while for the first time in the history of the two divisions the mortality of the second division was higher than that of the first, being 1·3%. It should be noted, however, that these were the identical results which Boer had achieved 50 years before by applying the principles he had learnt in Great Britain from Denham.

In the same year, 1847, another tragic event happened in the Vienna Lying-In Hospital. A pregnant woman with a fungating carcinoma of the cervix was admitted to a ward in which were 12 mothers; 11 of them died. The truth then dawned on Semmelweiss with its full force, namely that not only was the cadaver dangerous as a source of infection but even the living could be the primary focus from which this terrible disease could spread. Like the prodigal son Semmelweiss uttered his confession from the heart: 'I must confess that God only knows how many I have assigned to the grave. I have occupied myself with the cadaver to an extent reached by few other obstetricians.' He now taught that puerperal fever was a resorption fever brought about by the introduction of decomposed animal matter to the genitalia of a parturient woman. He stated further that this 'decomposed animal matter' could be transmitted from a corpse or from the wounds of the living. It could be carried on the hands, on linen, on instruments, on bedpans and even by the air. He stated further that it was but one form of pyaemia and that the surgeons should take heed of what was happening. This was in the year 1847, and today, when events of moment are flashed across the earth in a matter of seconds, it is sad to recall that it was 2 years before the views of Semmelweiss reached London. In 1849 they were proclaimed in that city and were generally accepted as being true. That same year Semmelweiss was dismissed from his post and, to complete the tragedy of his life, was later admitted to a mental asylum, where he himself died of pyaemia.

PASTEUR AND LISTER

The scene now changes as we leave the realm of medicine for a few moments and return to Great Britain and to the years referred to in the prologue. In 1774 a young Scot, James Watt, left Glasgow for Birmingham to join an industrialist and engineer called Matthew Boulton. Watt took with him great hopes and great ideas. In association with Boulton and with other scientists and engineers of the time he transformed these ideas into an invention of steam and steel and the first steam engine was created. This was the beginning of the Industrial Revolution. One result of this was that cities grew larger, accidents became commoner and hospitals for dealing with the trauma of industry were necessary on an ever-increasing scale. The days of frock-coated surgeons with blood and pus as the hall-marks of their skill had dawned. The Quaker surgeon, Joseph Lister, born in 1829, was appointed to the Chair of Surgery at Glasgow in 1860. The post-operative mortality from fever and gangrene following amputations was at times as high as 45%, and at one stage Lister was concerned lest surgery in institutions would have to cease. He knew of the Hippocratic concept of healing by first intention and realized that this occurred only when there was no putrefaction, but the problem to solve was how this putrefaction could be avoided. Meanwhile in France Louis Pasteur, who had been born 7 years before Lister, in 1822, was now a chemist and scientist particularly interested in the processes of fermentation of beers and wines. In 1854 he was Professor of Chemistry at Lille, where he was able to refute the growing theory of 'spontaneous generation' by showing that micro-organisms were in the atmosphere and were responsible for the fermentative processes in the production of wine and beer. It is interesting to note that among other substances he referred to *Penicillium glaucum*. In 1876 he published his paper '*Etude de la Bière*', and by this time Pasteur had realized and was teaching that the healing of living matter occurred by first intention when the body was protected from the micro-organisms to which he had drawn attention. He later studied cholera in chickens and reduced the mortality from 10% to less than 1%. The anthrax bacillus was then discovered and he investigated the production of immunity by means of attenuated strains.

The scene changes once more to Scotland, were Lister heard of the work of Pasteur and saw in it the answer to the problem which was giving him such grave concern. In 5 years the era of modern surgery had begun as Lister introduced his antiseptic techniques. He was appointed Professor at Edinburgh in 1877 and later went to King's College, London, where Cheatle was his house-surgeon. He had effected a surgical revolution, but not without opposition, and some of the great men of his time were bitterly opposed to his new ideas. Men like Fothergill, who at times smoked a pipe when performing the operation which has made him famous, believed that 'kitchen cleanliness' was all that was necessary and one must pay tribute to the excellent results these men achieved. Others, like Lawson Tait, were more actively hostile, but it is recorded that Lister was more saddened than angered by the failure of colleagues to see the evidence which, as he said to Cheatle, was so clearly displayed before their eyes. It will be appreciated that the history of puerperal fever cannot be fairly reviewed without paying tribute to those great men who, in fields other than obstetrics, made the contributions which have meant so much to mankind, just as in the first instance early obstetrical pioneers were the ones who showed the road to the surgeons by which the great enemy to surgery could be overcome.

Droplet Infection

The next page in the history of the conquest of infection was again written by a surgeon in the early years of the 20th century, when Halstead conceived, practised and taught his new ideas of aseptic surgery. His clinic in America was visited by young surgeons from many parts of the world, including men like Sargent from St. Thomas's Hospital, London. When these men returned to their own units their newfangled ideas were not always received favourably by their more senior colleagues, but the results achieved

proved their worth and more and more surgeons sought to understand the methods involved. In the 1930s the teachings of Denham and of Oliver Wendell Holmes so many years before were given a new emphasis by the work of Colebrook and his associates, when they demonstrated the importance in obstetrics of the haemolytic streptococcus and of the need to wear masks, and to wear them intelligently, and of the dangers of droplet infection. There are unfortunately still some who either do not wear masks at all or, even worse, wear them dangerously. There has recently been made available in England a film for teaching purposes demonstrating a normal delivery. It is perhaps relevant to our topic to make the comment that the obstetrician as he delivers the baby is not wearing a mask but the nurse who comes in later to bring a cup of tea to the happy mother with the baby in her arms is properly gowned and masked. This film was made in a South African hospital.

CHEMOTHERAPY AND ANTIBIOTICS

At the time that Colebrook and his colleagues were working with the haemolytic streptococcus, the first of the sulpha drugs—red sulpha—became available. There is no need to enlarge on the tremendous developments which followed in the field of chemotherapy but it is of interest to note that in England and Wales the Registrar-General's figures show that the maternal mortality from puerperal sepsis fell within a relatively few years to one-thirteenth of what it had previously been.

The next chapter in the history of the battle against infection was opened when a lady who was herself a doctor and the wife of a professor of pathology requested permission of the authorities at Oxford to test in the wards of the Radcliffe Infirmary a new preparation which had been isolated and prepared by her husband in the laboratories of that city. This early trial of penicillin restored to life patients desperately ill with infections of many types, including some with gas gangrene. In spite of the miracles which happened before the eyes of those of us who were privileged to see some of these early trials it is doubtful whether Lady Florey, as she later became, or any one of those associated with her, realized at that early stage just how significant the contribution was which they were making to the field of medicine and to mankind. In those early flasks and in the preparations which were soon developed Man was not only given the cure for the pyogenic infections but he was handed the weapons with which he could overcome the plagues and the pestilences which had ravaged the earth since the beginning of history. It is only a few years since these remarkable discoveries were made, but already we have seen a revolution in obstetrics as well as in other branches of medicine. Many fever hospitals are being closed and others are used for purposes for which they were not originally designed. We must remember, however, that the old dangers of puerperal fever have not been entirely removed and new ones have been developed with the advent of resistant strains of organisms. This provides us with a challenge to use the new weapons intelligently, to retain our clinical sense, to be constantly on our guard.

CONCLUSION AND EPILOGUE

There are many of you present who will live to write the date January 1st, the year 2000, on your notepaper. You will see great changes in many walks of life, and in medicine many of the modern techniques of which we now are proud will then seem obsolete. I trust, however, that there will be some who will pause from time to time in the rush of everyday living to look once more at the milestones of the past, to realize the lessons that were learned and the price that was paid for their learning. I trust that all of you will keep open, critical minds, constantly searching for truth itself and remaining free from personal antagonisms against those who have contrary views.

When there is a prologue there should be an epilogue and mine will be very brief. In the very early days of chemotherapeutic trials at Oxford a young and lovely woman was admitted to one of my beds desperately ill with a septic abortion. She had been taken to an abortionist in London and within 12 hours of her visit to him she was admitted to hospital apparently moribund. She had a triple septicaemia due to *Staphylococci*, *Bacillus coli* and *Clostridium welchii*. One million units of penicillin, which at that time was a dose of astronomical proportions, was given intravenously as the initial line of treatment, combined with drugs to combat her adrenal and renal failure. We knew that the coliform infection would not be touched by the penicillin and because of the anuria were unwilling to give sulpha drugs. We endeavoured to obtain some of the new preparation, streptomycin, which was then on the secret list and was being used by the Medical Research Council for a clinical trial in the treatment of tuberculous meningitis. We failed, but one of my registrars, seeing my concern, promised that if I would not ask where he got it from I should have a supply of the drug within a very short time. His promise was fulfilled and this patient was probably one of the first in the world to receive streptomycin for a condition other than tuberculous meningitis. Her condition improved and the kidneys started to function. Unfortunately she developed a huge subphrenic abscess caused by a penicillin-resistant staphylococcus, and even when this was drained she failed to rally. By this time, after weeks of suffering, her condition was desperate and even the most devoted nursing failed to prevent the skin from breaking over areas of pressure. Death seemed imminent. It was early Spring and one morning as I went into the ward to see if the lassie was still alive the sun was shining outside, the crocuses were appearing in the grass and the birds were singing. I said to the Sister, 'Let us take Hazel's bed out in the sun for a few minutes; the beauty of the morning may bring her some comfort'. This was done. Her courage was renewed and from that morning her progress was rapid and uneventful. Some years later she was happily married and after a year or two was safely delivered of a babe which has helped her to forget the tragedy of the past. The purpose of this epilogue is to remind us that the strength of the spirit cannot be measured by material standards, and that above all in medicine in the midst of scientific progress we must not lose the art of living nor an appreciation of things we cannot understand.

ASIAN INFLUENZA IN SOUTH AFRICA

The 'Asian' strain of influenza A virus has been isolated from cases in the outbreak of influenza in the Kaya Mandi Native location at Stellenbosch, Cape. This was announced on 7 August by Dr. A. Kipps, Acting Head of the C.S.I.R. Virus Research Unit of the University of Cape Town, where the isolation was conducted.

The virus was identified with the Asian strain supplied to the Unit by the World Influenza Centre in London by means of the haemagglutination inhibition test with ferret immune-serum, and a sample of the Stellenbosch virus has been supplied to the World Influenza Centre, London, for reference purposes.

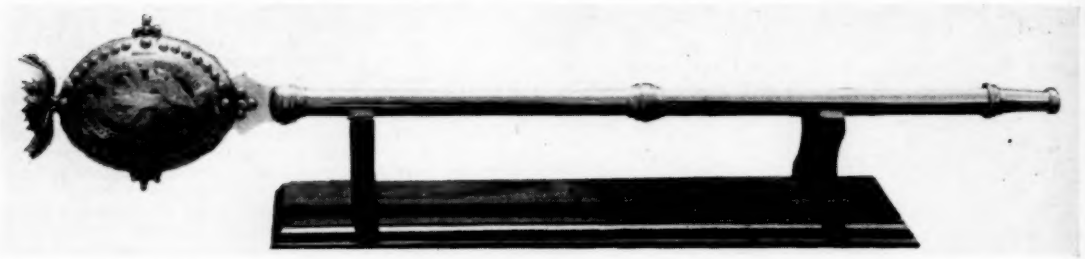
The influenza epidemic in South Africa is at present, in the majority of cases, taking the form of a febrile attack with severe headache; in some cases it is associated with sore throat or cough. In about 5 days the patient is commonly fit to return to work, and the attack is not followed by any conspicuous debility. The disease spreads very rapidly and widely and is occurring most commonly in Natives, though the other ethnic groups are becoming affected to a growing extent.

In this respect the epidemiology resembles that of the outbreak in Malaya, where, especially in the early stages, the majority of patients were poorer Asians in the most crowded and least healthy environment. However, in the 4th and 5th weeks of the Malayan epidemic more and more patients from the upper class of Asians and among the Europeans were seen. (S. Afr. Med. J., **31**, 732).

Several Branches of the Medical Association of South Africa have called for medical volunteers to assist the local authorities to meet epidemic emergencies by attendance at centres or by domiciliary visiting.

Vaccine prepared from the Asian influenza virus by the South African Institute for Medical Research is now available for the personal inoculation of general practitioners in private practice. Supplies of the vaccine have been sent to the Secretary of each Branch of the Medical Association of South Africa, to whom such practitioners should apply. (See page xxi of this issue.)

THE MACE OF THE MEDICAL ASSOCIATION OF SOUTH AFRICA



The mace was originally a weapon of offence. It was carried into battle by mediaeval bishops instead of the sword so that they could observe the canonical rule which forbade priests to shed blood.

About the middle of the 13th century ceremonial maces became established in France and England and were borne by sergeants-at-arms whose members formed royal bodyguards. Thereafter civil and ecclesiastical authorities as well as Parliaments, Universities and other important groups began to use the large mace at special gatherings as the symbol of authority. As time went on these maces were enriched with costly metals and embellished with heraldic and other devices and in certain cases were elaborately ornamented by skilled craftsmen.

It was felt to be fitting and desirable that in the Medical Association of South Africa symbolic evidence of properly constituted authority should be provided and a mace was accordingly instituted. The new mace carried the symbols which are incorporated in the Presidential Regalia—The Rod of Aesculapius (the Greek God of Healing) and the inscription

Societas medicorum Africae Australis

The appropriate floral emblem mounting the crest is that of a protea. The mace itself has been fabricated in South Africa and was presented to the Medical Association of South Africa by the Northern Transvaal Branch on the occasion of the Pretoria Congress in 1955.

A NEW TYPE OF GENERAL PRACTITIONER IN THE NETHERLANDS?*

If everything happens as planned, the new polders now being reclaimed from the former Zuyder Zee will be witness of an interesting experiment in medical care. It is a new plan, requiring the cooperation of the Netherlands Medical Association and the public health authorities, who, thus far, are in favour of trying it out.

By reclaiming entirely new areas from the sea, Holland is in a favourable position to try out a number of projects under expert supervision, based on extensive planning. By dint of careful soil tests the Dutch know beforehand exactly what type of soil they are going to find once their polders are dry, and their engineers know precisely how to condition the land for agricultural use. But long before the land is ready for the first inhabitants, the planners have been at work; as a result, the location and number of farms, towns, villages, churches, schools, hospitals, streets, roads, canals, and all such essentials, are actually mapped out and ready for inspection by prospective settlers when the waves are still rippling over the land-to-be.

This planning may seem very much like regimentation, but a country as overpopulated as the Netherlands must use every inch of its soil efficiently and, as a matter of fact, the result has made it impressively clear in the two new polders already in operation, that people are very satisfied. It is, therefore, not surprising that imaginative and idealistic people in all fields of endeavour are ever deliberating how to experiment in these new areas, so that they eventually may improve the country as a whole, and perhaps even the world.

One of these experiments deals with public health. In this respect it is evident that general practitioners, owing to their contact with all people, are the logical source of information on national health. But on the whole they are, especially in Holland, where partnership of doctors is unknown, a rather overworked, understaffed group of people, who have little time to read up on medical progress; and they can never, or hardly ever, devote sufficient time to periodical check-ups of all their patients, which is to the detriment of national health. To accept this simple truth as a premise seemed unethical to some progressive doctors, and the future communities of the Zuyder Zee polders gave them much food for thought. As a result, a committee was brought into being, consisting of members of the Royal Netherlands Society for the Advancement of Medicine. It was commissioned to study the prospective status of medical care in the future polders. This was in 1954, and just recently the report was published. It is a carefully worded report, written with mixed feelings, for the committee came to certain conclusions, whereby the freedom of practice of the individual GPs and their independence of all interference was somewhat at issue. Nevertheless, the group of doctors advises that the medical profession endorse the experiment, believing it to be of national importance that GPs play a bigger role in public health than is now the case.

The task of the future polder-GPs is envisaged as follows: to provide direct medical care where needed; check-ups of all their patients at regular intervals, whether sick or healthy; coordination with specialists, hospitals and school physicians regarding antenatal check-ups, paediatric and old-age care, and specialized treatments; and, finally, to gather the data obtained and file them systematically at a central point, for use in medical research and in furthering public health.

The drawbacks to this proposed experiment are obvious. Doctors would not be able to practise in the new polders wherever they would like to; they would have to do so in consultation with a planning committee. Their practice would be 30-40% smaller than usual. Part of their work would consist of rendering administrative service to a central body. In short—their cherished freedom would be somewhat curtailed.

The report advises that the logical body to plan, organize, and finance the experiment is the public board that promotes the interests of all new polder inhabitants—assisted and guided, of course, by a group of medical-association members and public-health officers.

Will prospective GPs be willing to cooperate in this new experiment? Among those who have been questioned thus far there seems to be a surprising number, especially of the younger physicians, interested and even eager to give it a try. For, although the Netherlands have the world's longest life expectancy and lowest death rate, it is generally felt that much more can be achieved in public health. The creation of new land provides the ideal surroundings for such an experiment.

* From the Netherlands Attaché for Press and Cultural Affairs, Pretoria.

NEW PREPARATIONS AND APPLIANCES: NUWE PREPARATE EN TOESTELLE

The Technique of Intramuscular Injection. Benger Laboratories Limited have published a 12-page commentary on the technique of intramuscular injection together with a photographic film strip illustrating the subject in colour.

The firm states that they have come to realize that the technique of intramuscular injection, especially among nurses, is sometimes faulty and that they have received a number of reports of skin staining following their intramuscular iron preparation *Imferon* resulting from faulty technique.

Messrs. Fisons Chemicals, associated with Benger's Limited state that they wish to distribute the film and commentary as widely as possible and would be only too pleased to supply a copy, free, to any sister tutor or other member of the medical or nursing professions. Application should be made to Fisons Chemicals (S.A.) (Pty.) Ltd., Triangle House, 226 Market Street (P.O. Box 5788), Johannesburg.

PASSING EVENTS : IN DIE VERBYGAAN

Mr. G. R. Crawshaw, M.D. (Vict.), F.R.C.S., recently of Johannesburg, has been appointed Honorary Cardiac and Thoracic Surgeon to the Bulawayo Group of Hospitals and is now in consultant practice at 807 Bradlow's Buildings, Abercorn Street, Bulawayo. Telephones: rooms 3366, residence 62947, Bulawayo.

* * *

W. G. Slate, M.C., M.B., Ch.B. (Cape Town), M.S. who for 2 years has served with the U.S. Army as Assistant Chief in the Obstetrics and Gynaecology Section, 16 Field Hospital, Nurnberg, Germany, has since 1 July 1957 joined the Department of Obstetrics and Gynaecology, University of Illinois, Chicago, as Assistant Professor under Professor William F. Mengert.

* * *

Mine Medical Officers' Association. At the General Meeting of the Transvaal Mine Medical Officers' Association held at Johannesburg on 18 July it was unanimously agreed to change the name of the Association to 'Mine Medical Officers' Association'. The reason for the change is that, owing to the growth of mining activities in the Orange Free State, mining medical officers are less exclusively confined to the Transvaal than hitherto.

* * *

Union of South Africa. Department of Health. Notification of formidable epidemic diseases and poliomyelitis in the Union during the period 26 July to 1 August 1957.

Poliomyelitis

	Fur.	*Nat.*	*Col.*	*Asiat.*	*Total*
Transvaal	1	–	–	–	1
Cape Province ..	4	2	3	–	9
Orange Free State ..	–	–	–	–	–
Natal	–	–	–	–	–
Totals	5	2	3	–	10

Plague, Smallpox, Typhus Fever: Nil.

REVIEWS OF BOOKS : BOEKRESENSIES

DISEASE IN CHILDHOOD

Disease in Infancy and Childhood. Second Edition. By Richard W. B. Ellis, O.B.E., M.A., M.D., F.R.C.P. Pp. vii + 710 with 393 illustrations. 50s. net. Postage 2s. Abroad. Edinburgh and London: E. & S. Livingstone Ltd. 1956.

Contents: I. History-taking and Examination. II. Social and Environmental Factors in Disease. III. Constitutional Factors in Disease. IV. The Newborn. V. Congenital Malformations. VI. Prenatal Infection. VII. Disorders of Nutrition and Digestion. VIII. Disorders of Storage. IX. Disorders of Growth and Development. X. Neoplastic Disease. XI. Disorders of the Blood. XII. Allergic Disorders. XIII. Rheumatic Disorders. XIV. Diseases of the Genito-urinary System. XV. Tuberculosis. XVI. Non-Tuberculous Disease of the Respiratoy Tract. XVII. Communicable Diseases and other Infections. XVIII. Degenerative and Miscellaneous Disorders. XIX. Behaviour Disorders. XX. Procedures and Therapy. Index.

In his preface, Professor Ellis reminds his readers that, although paediatrics is accepted as a separate branch both within and beyond the undergraduate curriculum, it should be remembered how closely this subject is connected with obstetrics and antenatal care, with the fields of general and preventive medicine, and with the broader scope of social medicine. Throughout the book Professor Ellis adheres to this concept and skilfully focuses attention on the manner in which paediatrics differs from general medicine: infantile defects of development; immaturity of response to disease; hazards linked with birth and growth; and the immunological and emotional inexperience of the growing child.

An interesting departure from custom is the description of diseases according to particular age-periods rather than as affecting particular systems. Thus the congenital malformations of all systems are discussed in one chapter and very well presented. Similarly neoplastic diseases, tuberculosis and other conditions involving various systems are dealt with in separate chapters.

As Professor Ellis states, this book is not intended as a comprehensive work of reference, and certainly it would not serve as such, but it is written as an introduction to clinical paediatrics for those who are already familiar with the natural history of disease processes in adults. In this role this work is most welcome and acceptable especially for undergraduates. The type and arrangement is excellent; bibliography and references are suitably grouped at the end of each chapter; and the illustrations are good and well produced, clearly showing what they are intended to demonstrate, which is not always the case in similar publications.

In a volume of this size, covering such a vast field, it would be surprising if there was no omission nor controversial statement. Indeed, in the opinion of the reviewer, such points of criticism can be found but are exceptional and, in any case, controversial so that these in no way detract from the great value of this book especially for undergraduates and practitioners anxious to improve their understanding and knowledge of modern paediatrics. The book is strongly recommended.

R.F.M

MEAT HYGIENE

Meat Hygiene. World Health Organization Monograph Series No. 33. Pp. 527. 106 Illustrations, 2 colour Plates. £2 10s. Geneva: World Health Organization. 1957.

Contents: Introduction. *Part I. Epidemiology.* The Epidemiology of meat-borne diseases—*C. E. Dolman. Part II. Ante-mortem Care.* Transport, ante-mortem care, and inspection of animals intended for slaughter—*M. J. J. Houthuis. Part III Slaughter.* Hygienic construction and technical organization of slaughter-houses—*G. Scaccia Scarafoni.* Methods of stunning, slaughter, and collection of blood—*T. Blom.* Electrical stunning—*Phyllis G. Croft.* The municipal abattoir—*R. Benoit Part IV. Post-mortem inspection.* General principles for post-mortem inspection and hygienic judgement of meat—*H. Thornton.* Post-mortem inspection and judgement of tuberculosis carcasses—*H. Drieux.* Post-mortem inspection and judgement of parasite-infected carcasses—*G. Schmid.* Application of bacteriological and biochemical tests in the hygienic judgement of meat and meat products—*A. Jepsen. Part V. Processing and marketing.* Hygienic aspects of

meat processing—*F. Schonberg.* Disposal and reclamation of by-products—*V. E. Albertsen.* Hygienic control of meat in markets and in food-serving establishments—*S. O. Koch. Part VI. Training of personnel.* Training of meat inspectors—*H. Thornton. Part VII. Meat-hygiene practice.* Survey of meat-hygiene practices in Europe—*R. I. Hood & H. H. Johansen.* Meat-hygiene problems in tropical areas—*M. M. Kaplan. Annexes:* 1. Meat consumption per annum (carcass weight) in certain European countries compared with that in Canada and the USA. 2. Netherlands regulations for road transport of slaughter animals. 3. Netherlands standards for transport abroad by rail of single-hoofed animals, horned beasts, sheep, and hogs. 4. Netherlands regulations for overseas transport of animals. 5. Directives for transport of animals by air. 6. Design of abattoirs. 7. Food-poisoning outbreaks in England and Wales, 1953, associated with processed and made-up meats. 8. Some characteristics of bacterial food-poisoning. 9. Specimen reporting-form for investigation of food-poisoning outbreaks. 10. Isolation and Identification of pathogenic bacteria in cases of food poisoning. 11. Enteric infections caused by *Shigella* and *Salmonella.* 12. Bacteriological examination of manufactures meat products. 13. Temperature control and salt treatment of meat containing trichinae or cysticerci. 14. Danish regulations for the judgement of meat: A. Judgement code on diseases and pathological conditions, 1949; B. Rules and instructions for laboratory methods of examination and their application in the hygienic judgement of carcasses, 1954. 15. Regulations of the Colony and Protectorate of Kenya for meat inspection. 16. Discussions at the WHO/FAO Seminar on Meat Hygiene. Select bibliography on meat hygiene. Index.

This comprehensive and well illustrated book contains contributions from experts who have spent a lifetime in the control of meat and its by-products.

All aspects of the meat industry, including reference to the hygienic handling and control of an article so liable to spoil, have received full and authorative consideration by the various contributors. Although this publication cannot be considered as an exhaustive treatise on this vast and intricate subject, it can be stated that the information presented is up to date and reflects in many instances the modern views of persons who have made their name as the leaders in the production and marketing of meat and its allied dairy products and their hygienic, bacteriological, and veterinary control.

It is surprising that the present-day problem of the design of suitable hygienic vehicles for the transportation of meat has received no mention.

It would be impossible to review in detail all the monographs which go to form this treatise. Each carries its own message and should be read in full. Reference is made to the use of water sprays before slaughter, and of electrical stunning methods, with a view to the production of a better-quality product; these should be experimented with in this country with a view to adoption.

The reviewer has recently had the opportunity of visiting certain abattoirs which are illustrated in this book and of personally consulting some of the contributors. The recommendation that all meat should be stamped after inspection appears strange to us in this country where this practice has with great success been in existence for very many years.

The quality of the paper is excellent, the print clear and legible, and the bibliography at the end of each monograph full and ample. The summary of the seminar which followed the presentation of the respective papers is, although abbreviated, sufficient to indicate the interest which had been aroused by all who attended. I have without hesitation to recommend this publication to all health officers, veterinary officers and medical officers of health. Its careful study will be more than amply repaid.

E.D.C.

DEVELOPMENTAL ABNORMALITIES OF THE EYE

Developmental Abnormalities of the Eye. Second Edition, Revised and Enlarged. By Ida Mann, C.B.E., M.A. (Oxon.), D.Sc., M.B., B.S. (Lond.), F.R.C.S. (Eng.), F.R.A.C.S. Pp. xi + 419. 284 Figures. 90s. net. London: British Medical Association. 1957.

Contents: Foreword to First Edition. Preface to Second Edition. Preface to First Edition. Acknowledgement. I. Origin of Developmental Abnormalities. II. Deformities of the skull Involving the Orbits. III. Abnormalities Affecting the Eye as a Whole. IV. Abnormalities of the Fundus Oculi (excluding Coloboma of Retina and Choroid and Retinal Cysts). V. Abnormalities of the Fundus Oculi (continued). VI. The Iris. VII. The Iris (continued). VIII. The Lens. IX. The Cornea. X. Abnormalities of the Conjunctiva and Sclera. XI. The Lids, Lacrimal Apparatus and Orbital. Contents. XII. The Management of Patients with Congenital Abnormalities. Bibliography. Index.

The subject matter of this book is ordinarily only of interest to the ophthalmologist and he will welcome this second edition of an already established classic. When it first appeared, the book was immediately accepted as an authoritative reference book of this branch of ophthalmology. The second edition, whilst remaining such, is no mere 'catalogue of aberrations', but an attempt is made to explain their mechanism and to illustrate them with excellent photographs of cases, with the pathological picture clearly demonstrated.

Though there are fewer pages than in its predecessor, this is due to there being more lines to the page and more words to the line. The content has actually been increased, partly by the extension of sections such as skull deformities and macular dystrophies, and partly by the addition of completely new material, such as toxoplasmosis, rubella cataract, retrolental fibroplasia and congenital vascular veils in the vitreous. There is an extra chapter on the management of these unfortunate cases.

This book thus remains a reference book essential to every Ophthalmologist. It can be opened at any page and useful information can be obtained about many conditions, some of which are of common occurrence while others are only encountered in the pages of this book.

L.S.

FAMILY MENTAL HEALTH

Family Mental Health and the State. Proceedings of the 8th Annual Meeting of the World Federation for Mental Health, Istanbul, August 1955. Pp. 165. 15s. net. London: H. K. Lewis & Co. Ltd. 1957.

Contents: Committee of Honour, Organizing Committee and Executive Board of W.F.M.H. Introduction. *Proceedings of the Annual Meeting. Part One. Inaugural Ceremony.* Address by *Dr. Behcet Uz, Minister of Health and Social Welfare.* Address by *Ord. Prof. Dr. F. K. Gokay, Governor-Mayor of Istanbul.* Presidential Address: The Peaceful use of Human Power. *Dr. Frank Fremont-Smith, President W.F.M.H. Part Two. Mental Health and Family Life.* Mental Health and the Upbringing of Small Children. *Dr. Kenneth Soddy.* The Problem of Children Deprived of Normal Family Life. *D. E. Novan and Dr. H. Bliginet.* The Family as a Factor in Juvenile Delinquency. *Prof. Nurullah Kunter.* Consideration of Certain Aspects of the Dynamics of Family Life in the U.S.A.: Report by a Study Group. *Dr. Janet Rioch.* The Reactions and Attitudes of Families towards their Physically and Mentally Handicapped Children. *Dr. A. Repond.* Mental Hygiene in the Home. *Prof. Dr. A. C. Pacheco e Silva.* The Health of Families in French Rural Areas. *Dr. Pierre Doussinet. Part Three. Child Study.* Stress: A Motion Picture on Emotional Stress and its Consequences. *Dr. René Spitz. Part Four. Education.* Mental Health and Education. *Cato Hambro, M.A., M.Ed.* The Place of Education in the Development of the Mental Health of Children of Pre-School and School Age. *Dr. Baha Arkan.* Special Education in Turkey. *M. Enc. Part Five. Cultural Change.* Life Stress and Health in a Changing Culture. *Rhoda Metraux, Ph.D. Part Six. The United Nations and Specialized Agencies.* United Nations Activities in Social Welfare in the Middle Eastern Region. *Ernest C. Grigg.* The Work of the World Health Organization. *Dr. Brock Chisholm. Part Seven. Closing Session.* Summing-up. *Prof. Dr. H. C. Rumke.* Observers of Other Organizations. Composition of Discussion Groups. Representation of Member-Associations of W.F.M.H. Participants. Secretariat of W.F.M.H.

Symposia usually make dreary reading, and this one is no exception. The compressed space seems to stifle new ideas at birth and makes the old ones dull and trite, and yet one must be grateful that in this uneasy world medical men have met and discussed, without attrition, problems to do with mental health in the family and in childhood, and problems in education and in changing cultures. As Dr. Fremont-Smith says in his Presidential address, 'The control of atomic power is not central in the great issue of war or peace any more than fever is central in the issue of sickness or health . . . . The threatening display of atomic weapons is a symptom, but not the cause, of a deep-seated social malaise and sickness among nations which threatens human survival.' A sentiment not less true because these words, spoken in the WFMH, reach only ears west of the iron curtain.

Amongst the most interesting papers is one by Margaret Mead describing the complete change in style of life and in habits amongst the Manus of the Admiralty Islands which occurred in 20 years. The energy, she states, was 'provided by the people's unrealized aspiration . . . towards a society in which people would work together without continual anger and quarrelling.' This energy completely transformed a semi-savage society into a modern one in the time usually given to the education of a Western man. But before jumping to rash conclusions one must (as Dr. Mead herself points out) ask: What changes do the people want? What changes does the inhabitant of Europe want? What changes does the South African want? These questions must follow on Dr. Mead's surmise and might lead to altered viewpoints in many of those who feel they have an answer to problems in racial developments.

Not all the speakers chose such wide subjects; much space is devoted to less controversial aspects of Mental Health and Education and even to the causes of broken marriages, and although dulness is not lacking, neither is sincerity and goodwill.

J. MacW. MacG.

BOOKS RECEIVED : BOEKE ONTVANG

The Year Book of the Eye, Ear, Nose and Throat. (1956-1957 *Year Book Series.*) *The Eye.* Edited by Derrick Vail, B.A., M.D., D.Oph. (Oxon.), F.A.C.S., F.R.C.S. (Hon.). *The Ear, Nose and Throat.* Edited by John R. Lindsay, M.D. Pp. 448. 128 Illustrations. $7.00 post paid. Chicago: Year Book Publisher, Inc. 1957.

An Atlas of Muscle Pathology in Neuromuscular Diseases. By J. Godwin Greenfield, M.D., G. Milton Shy, M.D., Ellsworth C. Alvord, Jr., M.D. and Leonard Berg, M.D. Photomicrographs by Fred. H. Meiller. Pp. ix + 104. Illustrations, some in colour. 45s. net + 10d. Postage Abroad. Edinburgh and London: E. & S. Livingstone Ltd. 1957.

Recent Outbreaks of Infectious Diseases. By S. Leff, M.D., D.P.H. Pp. xii + 408. 2 Illustrations. £1 15s. net. London: H. K. Lewis & Co. Ltd. 1957.

The Essentials of Materia Medica Pharmacology and Therapeutics. Seventh Edition. By R. H. Micks, M.D., F.R.C.P.I. Pp. x + 432. 28s. net. London: J. & A. Churchill Ltd. 1957.

The Principles of Therapeutics. By J. Harold Burn, M.A., M.D., F.R.S. Pp. ix + 278. 36 Figures. 27s. 6d. Oxford: Blackwell Scientific Publications. 1957.

Chronic Bronchitis in Newcastle-Upon-Tyne. By A. G. Ogilvie, M.D. (Dunelm), F.R.C.P. (Lond.) and D. J. Newell, M.A. (Cantab.). Pp. vii + 115. 6 Figures. 15s. net + 9d. Postage Abroad. Edinburgh and London: E. & S. Livingstone Ltd. 1957.

Privy Council. Medical Research Council Memorandum No. 34. *The Treatment of Wound Shock—The Wound Shock Working Party.* Pp. vii + 39. 4 Figures. 3s. 6d. net. London: Her Majesty's Stationery Office. 1957.

Treves' Surgical Applied Anatomy. Thirteenth Edition. Revised by Lambert Charles Rogers, M.D., M.Sc., F.R.C.S., F.R.C.S.E., F.R.A.C.S., F.A.C.S. Pp. x + 591. 202 Figures. 30s. net. London: Cassell and Company Limited. 1957.

Human Cancer—A Manual for Students and Physicians. By Maurice M. Black, M.D. and Francis D. Speer, M.D., F.C.A.P. Pp. 273. 34 Figures. $7.50. Chicago: Year Book Publishers, Inc. 1957.

An Atlas of the Commoner Skin Diseases. Fifth Edition. By Henry C. G. Wilson, M.A., D.M. (Oxon.), F.R.C.P. (Lond.). Revised with the collaboration of Harold T. H. Wilson, M.A., M.D. (Cantab.), M.R.C.P., D.T.M. Pp. viii + 375. 153 Colour Plates. 105s. post 1s. 6d. Bristol: John Wright & Sons Ltd., Medical Publishers. 1957.

Principles of Urology. An Introductory Text-book to the Diseases of the Urogenital Tract. By Meredith F. Campbell, M.S., M.D., F.A.C.S. Pp. xxii + 622. 319 Figures. $9.50. Philadelphia and London: W. B. Saunders Company. 1957.

Excerpta Medica. The International Medical Abstracting Service.

Cardiovascular Diseases. Vol. I. No. 1. Section XVIII. January 1957. (Abstr. No. 1—303). Editor: J. W. C. de Groot. Pp. 78. Each yearly volume will contain 800 to 900 pages inclusive of the yearly authors' index and a cross-referenced subject index. Subscription fee $15 per year. Amsterdam: The Excerpta Medica Foundation. 1957.

Extensile Exposure. Second Edition. By Arnold K. Henry, M.B., (Dublin), M.Ch. (Hon.), Trinity College, Dublin and Cairo, F.R.C.S.I. Chevalier de la Légion d'Honneur. Pp. xii + 320. 298 Illustrations. 45s. net + 1s. 5d. Postage Abroad. Edinburgh and London: E. & S. Livingstone Ltd. 1957.

Bedside Diagnosis. Fourth Edition. By Charles Seward, M.D., F.R.C.P. (Edin.). Foreword by Lord Cohen of Birkenhead, M.D., D.Sc., LL.D., F.R.C.P., F.A.C.P., F.F.R. Pp. xxiv + 430. 21s. net + 10d. Postage Abroad. Edinburgh and London: E. & S. Livingstone Ltd. 1957.

Trophoblastic Growths. Aclinical, Hormonal and Histopathologic Study of Hydatidiform Mole and Chorionepithelioma. By J. Smalbraak, M.D. Pp. viii + 342. 66 Plates (8 in color) and 9 tables. 72s. Amsterdam, London, New York, Princeton: Elsevier Publishing Company. 1957. Sole Distributors for the British Commonwealth except Canada: Cleaver-Hume Press Ltd., London.

Year Book of Orthopedics and Traumatic Surgery 1956-1957 *Series.* Edited by Edward L. Compere, M.D., F.A.C.S. F.I.C.S. Pp. 336. 208 Figures. $6.75. Chicago: Year Book Publishers, Inc. 1957.

The Bright Countenance. A Personal Biography of Walter Morley Fletcher. By Maisie Fletcher. Pp. 351. 11 Illustrations. 25s. net. London: Hodder and Stoughton. 1957. Local Sales Agent: Howard B. Timmins, 109 Long Street, Cape Town.

Atlas of Clinical Endocrinology. Including Text of Diagnosis and Treatment. By H. Lisser, A.B., M.D. and Roberto F. Escamilla, A.B., M.D. Pp. 476. 148 Illustrations, including 3 in colour. South African Price £8 0s. 6d. St. Louis: The C. V. Mosby Company. 1957.

Study Group on the Ecology of Intermediate Snail Hosts of Bilharziasis: Report. World Health Organization: Techincal Report Series, 1957. No. 120, 38 pages. Price, 1s. 9d. Also available in French and Spanish. Local Sales Agent: Van Schaik's Bookstore (Pty.) Ltd., P.O. Box 724, Pretoria.

Study Group on atherosclerosis and ischaemic heart disease: Report. World Health Organization: Technical Report Series, 1957, No. 117, 40 pages. 1s. 9d. Also available in French and Spanish. Local Sales Agent: Van Schaik's Bookstore (Pty.) Ltd., P.O. Box 724, Pretoria.

Official Records of the World Health Organization. No. 75.

The Work of WHO 1956. Annual Report of the Director-General to the World Health Assembly and to the United Nations. Pp. xi + 233. 5 Maps. Illustrations. 10s. Also available in French and Spanish. Geneva: World Health Organization. 1957. Local Sales Agent: Van Schaik's Bookstore (Pty.) Ltd., P.O. Box 724, Pretoria.

Fluid Balance in Surgical Practice. 2nd Edition. By L. P. le Quesne. 20s. net. Pp. vii + 140. London: Lloyd-Luke (Medical Books) Limited. 1957.

The Premature Baby. 4th Edition. By V. Mary Crosse. Pp. x + 242. With 39 illustrations. 20s. net. London: J. & A. Churchill Ltd. 1957.

Medical Ethics. A Guide to Students and Practitioners. Edited by Maurice Davidson, D.M. (Oxon.), F.R.C.P. (Lond.). Pp. viii + 165. 1 illustration. 20s. net. London: Lloyd-Luke (Medical Books) Ltd. 1957.

An Introduction to Blood Group Serology. By Kathleen E. Boorman, Senior Scientific Officer, South London Blood Transfusion Centre and Barbara E. Dodd, M.Sc. (Lond.), Ph.D. (Lond.) Pp. viii + 317. 30 illustrations. 40s. net. London: J. & A. Churchill Ltd. 1957.

The Principles and Art of Plastic Surgery. Volumes 1 and 2. By Sir Harold Gillies and D. Ralph Millard Jr. Pp. xxi + 317. With illustrations. £12 10s. 0d. + 3s. 10d. Postage. London: Butterworth & Co. (Publishers) Ltd. South African Office: Butterworth & Co. (Africa) Ltd., P.O. Box 792, Durban. 1957.

Gout. John H. Talbott, A.B., M.C., D.Sc. (Hon.). Pp. xvi + 205. 16 Colour plates and 63 graphs and illustrations. New York: Grune & Stratton, Inc. 1957.

Tumors of the Kidney, Renal Pelvis and Ureter. By Balduin Lucké and Hans G. Schlumberger. 208 pages and 187 illustrations and diagrams. Washington: Armed Forces Institute of Pathology. 1957.

Tumors of the Pituitary Gland and Infundibulum. By James W. Kernohan and George P. Sayre. Pp. 81. 67 illustrations. $1.00. Washington: Armed Forces Institute of Pathology, 6825 16th Street, N.W., Washington 25, D.C., D.C. 1956.

Tumors of the Eye and Adnexa. By Algernon B. Reese. Pp. 205. 122 illustrations. Washington: Armed Forces Institute of Pathology. $2.00. 1956.

Practical Refraction. By B. C. Gettes. Pp. vi + 170. 57 diagrams and illustrations. $6.50. New York: Grune & Stratton, Inc. 1957.

Fluorine in Water Supplies. The Fluoridation of public Water Supplies. By Douw G. Steyn.

Aids to Pathology. Eleventh Edition. By John O. Oliver, M.B., B.S. (Lond.), M.R.C.S. (Eng.), L.R.C.P. (Lond.). Pp. viii + 347. 10s. 6d. London: Baillière, Tindall & Cox Ltd.

Whillis's Elementary Anatomy and Physiology. Fourth Edition. By Roger Warwick, B.Sc., Ph.D., M.D. Pp. vii + 274. 107 illustrations. London: J. & A. Churchill Ltd. 1957.

Black Magic and White Medicine. A Mine Medical Officer's Experiences in South Africa, the Belgian Congo, Sierra Leone and the Gold Coast. By Michael Vane. Pp. 254. 5 illustrations. 16s. London and Edinburgh: W. & R. Chambers Ltd. 1957.

Endemic Syphilis in the Bakwena Reserve of the Bechuanaland Protectorate. Bulletin 15. By J. F. Murray, A. M. Merriweather, M. L. Freedman with D. J. de Villiers. Pp. 975-1039. 76 illustrations. Geneve: World Health Organization. 1956.

CORRESPONDENCE : BRIEWERUBRIEK

THE J. D. ALLEN MEMORIAL FUND

To the Editor: A fund has been opened to perpetuate the memory of the late Dr. J. D. Allen (First Superintendent of Baragwanath Hospital). The memorial will take the form of a postgraduate prize for nurses, an incentive prize for the best non-European worker and a bird-bath to be erected in front of the new theatre block, which is to be named after Dr. Allen.

As there may be among your readers some who had the privilege of working under Dr. Allen, it is felt that they might wish to be associated with the memorial. If so would they be kind enough to send their contributions to the J. D. Allen Memorial Fund, Baragwanath Hospital, Johannesburg.

I. Frack
Medical Superintendent

Baragwanath Hospital
Johannesburg
3 August 1957

DIE J. D. ALLEN-GEDENKTEKENFONDS

Aan die Direkteur: 'n Fonds is gestig om die gedagtenis aan wyle dr. J. D. Allen (Eerste Geneeskundige Superintendent van Baragwanath-hospitaal) te verewig. Die gedenkteken sal die vorm aanneem van 'n na-graadse prys vir verpleegsters, 'n aanmoedigende prys vir die beste nie-Blanke werker en 'n voëlbad wat voor die nuwe teaterblok, wat na Dr. Allen vernoem word, opgerig sal word.

Indien daar miskien enige van u lesers is wat die eer gehad het om onder Dr. Allen te werk, en wat begerig is om hulle met die gedenkteken te vereenselwig, sal dit waardeer word as bydrae aan die J. D. Allen-gedenktekenfonds, Baragwanath-hospitaal, gestuur kan word.

I. Frack
Geneeskundige Superintendent

Baragwanath-hospitaal
Johannesburg
3 Augustus 1957

MEDICAL FEES IN BLOOD TRANSFUSION

To the Editor: At its next meeting, the Federal Council will consider the possibility of laying down a uniform scale of fees throughout the Union with regard to blood transfusions. This will apply, not only to the cost of each bottle of blood, but also to the medical fees in connection with the administration of the blood and the various serological tests, such as the grouping of patients, compatibility tests, etc.

The National Voluntary Blood Donors Association has indicated that the expense to the patient for blood transfusions (including all the tests that are required) should be made as low as possible. The Donors have expressed the view that, since they gave their blood free and would give as much as was necessary, the doctors should make a concession to their patients, and they felt also that blood transfusions could not be compared with any other medical procedure because of the cooperation of this voluntary association.

Unfortunately, the National Voluntary Blood Donors Association has overlooked the fact that, although blood donors actuated by the highest motives give their blood as an act of charity, their livelihood does not depend upon it. The administration of blood and all that goes with it is part of the daily work and livelihood of the doctors concerned. It has always been the aim of our profession to consider the financial position of patients, and I feel that the assessment of fees should be left to the discretion of the doctors concerned and that each case should be judged on its merits.

During the last two decades, the use of blood as a therapeutic measure has increased steadily and progressively. Today many major surgical operations could not be carried out without it. The introduction and development of blood banks has very largely permitted this widespread use of blood in almost all branches of medicine. The major function of any blood transfusion service must be the maintenance of its blood bank, which of course includes all the organization and handling of the donors, as well as the storage of the blood and the preparation of plasma and serum.

This is an extremely complex organization, which for many reasons has to be centralized, with sub-banks scattered through the area surrounding it; and I feel that to burden the organization with the actual administration of blood is undesirable. It should be the aim of every blood transfusion service to make blood as readily available as possible to every medical practitioner who may require it.

The administration of blood, is not a simple mechanical matter, and only the doctor in charge of the case (whether general practitioner or specialist) can decide when, how much, at what rate, and in what manner, blood should be given. I feel that the aim of the blood transfusion services should be, not to develop closed panels of doctors acting as blood transfusion operators, however expert they may be, but to encourage the administration of blood by all members of the profession.

The importance of the compatibility tests on every individual bottle of blood cannot be over-emphasized. True, there are rare occasions when the immediate administration of Group-O blood to an exsanguinated patient *in extremis* is essential as a life-saving measure; under these conditions a delay in attempting to carry out grouping and compatibility tests cannot be considered. This type of case, however, is rare in civilian practice, and serves as the exception to the rule for a compatibility test for every bottle of blood.

The various techniques for compatibility tests have become more complicated and more sensitive with the passage of time. Gone are the days when a compatibility test consisted in mixing on a soup plate a drop of the patient's blood (usually whole blood and not serum) with a drop of the donor's blood and a drop of citrate solution. The result was read within 3 minutes, before the mixture dried out or, on occasion, coagulated. At the present day, the necessity of setting up compatibility tests in test-tubes incubated at 37°C for 2 hours is well recognized. The test should include mixtures of the recipient's serum with suspensions of the donor cells in both saline and some protein-rich medium, such as bovine albumin. On occasion an indirect Coombs test may be required as well. If transfusion reactions are to be reduced to the minimum, the use of complicated compatibility tests is essential.

I feel that it is in the interest of the patients for the full use of the services of clinical pathologists (who have specialized training in Serology) to be made wherever possible. The successful management of many patients depends on the team work of a number of specialists, all of whom are directly or indirectly concerned in the administration of blood to the patient.

Patients, like doctors, are individuals, and let us avoid regimentation, closed shops, and mass production organizations as much as possible.

Union-wide scales of fees are an ideal, but conditions and customs of practice differ in different areas, making it virtually impossible to arrive at a scale that will be acceptable to all.

W. G. Davis

'Ormonde'
2 Wood Road
Rondebosch, Cape
12 August 1957.